The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 141, No. 3 — CHICAGO, ILLINOIS — SEPTEMBER 17, 1949

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PAINLESS JAUNDICE

Chairman's Address

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A discussion of painless jaundice should be preceded by some qualification of the title. Pain is a subjective phenomenon for which there is no reliable gage, and its estimation is based on the patient's description and reactions. The great variations in degree of pain to what appears to be approximately the same stimulus are well known, and when the term painless is used it is to be interpreted in a relative sense. The scope of jaundice for the purposes of the present discussion is limited to the types directly related to the liver parenchyma and to the biliary passages.

TYPES OF JAUNDICE

Jaundice directly concerned with the biliary system falls into two principal classifications, (1) that due to injury of the liver cells by some form of infection or toxin, and (2) that caused by obstruction of the biliary passages.

When the parenchymal cells of the liver are at fault, jaundice is due to inability of the cells to collect and excrete the normal components of the bile. This leads to an accumulation in the serum of bilirubin which has not passed through the liver and consequently gives rise to an indirect van den Bergh reaction.[1] There is at the same time an increase of urobilin in the urine and feces. Rich [2] has classified this type as retention jaundice, the retention being due to inability of the liver cells to carry out their excretory function with respect to bile pigments.

In the purely obstructive type of jaundice the liver cells excrete the bile pigments, but an obstruction somewhere in the biliary passages prevents the normal flow of the bile into the duodenum. In this event there is reabsorption, or regurgitation, of bile into the blood, probably by way of the lymphatic vessels, and since the bile has passed through the liver cells the van den Bergh reaction is direct. Bilirubin and bile salts appear in the urine, and there is a decrease of urobilin in the feces. This type of jaundice is known as obstructive, or regurgitation, jaundice.[2]

DIFFERENTIATION

If an accurate history can be obtained and early clinical observations and laboratory investigations can be made, the differentiation of the infective or toxic type of jaundice is relatively simple. When a patient under 30 years of age presents himself with a short history of fatigue, general malaise, fever, nausea, upper abdominal discomfort (or it may be described as pain), vomiting and jaundice a presumptive diagnosis of infectious hepatitis is justified. Often there is a history of a cold or influenza occurring about two weeks before the onset. If the physical and laboratory observations are confirmatory, the diagnosis is established. Since the disease is self limited, recovery may be anticipated.

Complacency toward this form of relatively painless jaundice in young adults, however, was badly shaken during the reecnt World War. Through the desire to protect our soldiers against a variety of diseases occurring in the various parts of the world to which they might be sent, mass inoculations of pooled protective serums were given, particularly for the prevention of yellow fever. The inoculations were followed by the outbreak of a type of jaundice which had much in common with the ordinary epidemic acute hepatitis but differed from it to some extent by a longer incubation period, a longer duration, greater severity, greater tendency toward relapse and, in some instances, more disastrous consequences.

Whether acute infectious hepatitis and homologous serum hepatitis are one and the same disease has not been definitely established. Havens [3] found that an attack of serum hepatitis did not produce immunity against infectious hepatitis. Neefe [4] and his associates likewise were unable to demonstrate cross immunity between the two conditions. Watson and Hoffbauer,[5] however, point out that multiple attacks of catarrhal jaundice (infectious hepatitis) in the same person are well authenticated. Paul and Havens [6] apparently regard serum hepatitis as a variant of infectious hepatitis.

A point of practical importance pertaining to both forms of hepatitis is that certain patients sustain permanent damage to the liver. Kunkel [7] and his associates, in a follow-up study of 350 patients who had had hepatitis, found 60, or 17 per cent, who had not recovered in the usual manner. Two presented the clinical picture of severe cirrhosis. Soffer and Paulson [8]

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Read before the Section on Surgery, General and Abdominal, at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 9, 1949.

1. Schiff, L.: The Differential Diagnosis of Jaundice, Chicago, The Year Book Publishers, Inc., 1946.
2. Rich, A. R.: The Pathogenesis of the Forms of Jaundice, Bull. Johns Hopkins Hosp. **47**: 338-377 (Dec.) 1930.
3. Havens, W. P., Jr.: Experiment in Cross Immunity between Infectious Hepatitis and Homologous Serum Jaundice, Proc. Soc. Exper. Biol. & Med. **59**: 148-150 (June) 1945.
4. Neefe, J. R.; Stokes, J., Jr., and Gellis, S. S.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis: Experimental Study of Immunity and Cross Immunity in Volunteers, Am. J. M. Sc. **210**: 561-575 (Nov.) 1945.
5. Watson, C. J., and Hoffbauer, F. W.: The Problem of Prolonged Hepatitis with Particular Reference to the Cholangiolitic Type and the Development of Cholangiolitic Cirrhosis of the Liver, Ann. Int. Med. **25**: 195-227 (Aug.) 1946.
6. Paul, J. R., and Havens, W. P., Jr.: Recent Advances in the Study of Infectious Hepatitis and Serum Jaundice, Tr. A. Am. Physicians **59**: 133-141, 1946.
7. Kunkel, H. G.; Labby, D. H., and Hoagland, C. L.: Chronic Liver Disease Following Infectious Hepatitis: I. Abnormal Convalescence from Initial Attack, Ann. Int. Med. **27**: 202-219 (Aug.) 1947.
8. Soffer, L. J., and Paulson, M.: Residual Hepatic Damage in Catarrhal Jaundice as Determined by the Bilirubin Excretion Test, Arch. Int. Med. **53**: 809-813 (June) 1934.

also have described residual hepatic damage in patients who had had infectious hepatitis. It is conceivable that in future years diagnostic studies involving liver function tests may be complicated by permanent changes in the liver that have occurred after attacks of epidemic acute hepatitis or homologous serum jaundice.

TABLE 1.—*Icterus Index*

(Normal Value: 4 to 6 Units)

	No. of Cases	Range of Values	Average Value
Acute hepatitis	35	12.1 to 251.0	80.7
Cirrhosis	31	12.5 to 193.0	48.6
Acute cholangitis	3	11.0 to 83.4	40.3
Carcinoma of pancreas	25	18.2 to 160.0	90.1
Carcinoma of ampulla of Vater	2	13.0 & 78.0	45.5
Carcinoma of common or hepatic duct	2	145.0 & 178.0	161.0
Carcinoma of liver	5	8.6 to 109.0	48.2
Stone in common or hepatic duct	23	9.0 to 233.0	44.8

Surgical interest in the infectious or toxic types of jaundice, in which the liver cells are primarily concerned, is limited chiefly to its differentiation from the obstructive, or regurgitation, types. In addition to the clinical manifestations of the disease, differentiation is facilitated by certain laboratory examinations which will be discussed later.

The obstructive types of jaundice, on the other hand, almost invariably demand a consideration of surgical treatment of the underlying disease. Here again the clinical observations may find support in the laboratory. It is unfortunate, however, that there are no tests in which complete reliance can be placed for the identification of the different types of jaundice. They must be looked on as aids and not as definitive diagnostic methods. Once it is established with reasonable certainty that the jaundice is obstructive, the diagnosis must be carried a step further and a determination made as to whether the obstructing mechanism is in the extrahepatic ducts or concerns the cholangioles within the liver.

ETIOLOGIC CONSIDERATIONS

In the latter category Hanger and Gutman[9] have described jaundice following arsphenamine therapy, which was not of the usual hepatogenous type but

TABLE 2.—*Serum Bilirubin*

(Normal Value: 0.2 to 0.8 Mg. per Hundred Cubic Centimeters)

	No. of Cases	Range of Values	Average Value
Acute hepatitis	12	1.1 to 22.0	8.1
Cirrhosis	11	0.5 to 6.1	3.1
Acute cholangitis	2	2.5 & 12.3	7.4
Carcinoma of pancreas	3	6.1 to 12.0	9.2
Carcinoma of ampulla of Vater	0	.....	...
Carcinoma of common or hepatic duct	0	.....	...
Carcinoma of liver	4	1.9 to 13.7	7.8
Stone in common or hepatic duct	8	3.8 to 11.3	7.4

appeared to be due to obstruction of the intrahepatic biliary passages. In the cases reported, the laboratory criteria showed little evidence of degeneration of the liver cells. Watson and Hoffbauer[9] also described certain cases of jaundice in which there was relatively normal hepatocellular function in the presence of severe jaundice of the obstructive, or regurgitation, type. In their cases the histologic evidence appeared inadequate to indicate intrahepatic biliary obstruction, and they were of the opinion that the continued regurgitation of bile into the blood stream was due to increased permeability of the cholangioles.

Obviously it is not always possible to be sure whether the cause of an obstructive type of jaundice, as determined by laboratory methods, lies within biliary passages of the liver itself or in the extrahepatic ducts, and in a given case the advisability of surgical therapy must be determined on all the evidence available, both clinical and laboratory. Fortunately, the decision in the great majority of cases is not as complicated as the preceding reports of exceptional cases would suggest. In the final analysis, the principal problems are to determine, first, whether the jaundice is of the obstructive type, and second, if so, whether its cause is extrahepatic and therefore possibly amenable to surgical treatment.

If it can be established that jaundice is of the obstructive type, it may be fairly assumed, with certain exceptions, that the obstructing mechanism lies outside the liver. It then becomes necessary to consider the possible causes in order of their relative frequency and attempt to arrive at a working diagnosis.

TABLE 3.—*Cephalin-Cholesterol Flocculation Test of Hanger*

(Normal Reaction: Negative)

	No. of Cases	Range of Value	Average Value
Acute hepatitis	39	Neg. to 4+	3.4+
Cirrhosis	38	Neg. to 4+	2.5+
Acute cholangitis	3	All Neg.	Neg.
Carcinoma of pancreas	9	Neg. to 3+	0.7+
Carcinoma of ampulla of Vater	1	3+	3+
Carcinoma of common or hepatic duct	1	Neg.	Neg.
Carcinoma of liver	7	Neg. to 4+	1.7+
Stone in common or hepatic duct	20	Neg. to 4+	1+

1. *Carcinoma of the Pancreas.*—In a study of jaundice in 245 patients 40 years of age or more, Schiff[1] found neoplastic disease responsible for 42.6 per cent of the cases, hepatogenous disease for 38.9 per cent and calculi for 14 per cent. The remainder, 4.5 per cent, were due to miscellaneous and undetermined causes. Carcinoma of the head of the pancreas is usually considered a painless disease. In many instances jaundice appears prior to the development of pain, but pain at some stage of the disease is by no means uncommon.[10] It is often described as dull, boring, nagging or burning, but the important point is that it usually does not have the characteristics of pain caused by cholecystic disease or stone in the common duct. Other subjective symptoms, such as weakness, anorexia and nausea, are similar to those caused by less serious diseases but as a rule are more insidious in their development. Physical examination may reveal enlargement of the gallbladder as described by Courvoisier.[11] The laboratory data shown in the tables are characterized by high icteric index, high phosphatase and in the early stages of the disease a relatively low cephalin flocculation (Hanger)

9. Hanger, F. M., Jr., and Gutman, A. B.: Postarsphenamine Jaundice Apparently Due to Obstruction of the Intrahepatic Biliary Tract, J. A. M. A. **115**: 263-271 (July 27) 1940.

10. (*a*) Bourne, G.: Pain as the Only Sign of Pancreatic Carcinoma, Lancet **2**: 1326-1327 (Dec. 5) 1936. (*b*) Zollinger, R., and Kevorkian, A. Y.: Surgical Aspects of Obstructive Jaundice, New England J. Med. **221**: 486-488 (Sept. 28) 1939. (*c*) Whipple, A. O.: Diseases of the Pancreas, in Nelson's Loose-Leaf Medicine, New York, Thos. Nelson & Sons, 1945, vol. 5, p. 531, Walters, W., and Snell, A. M.: Diseases of the Gall Bladder and Bile Ducts, Philadelphia, W. B. Saunders Company, 1940, p. 321.

11. Courvoisier, L. G.: Casuistich-statistische Beitraege zur Pathologie und Chirurgie der Gallenwege, Leipzig, F. C. W. Vogel, 1890.

reaction. The prothrombin activity, which is decreased, responds to vitamin K, if administered before severe damage to the liver cells has occurred.

II. *Carcinoma of the Common or Hepatic Duct.*—The symptoms, signs and laboratory data in carcinoma of the main biliary ducts are practically indistinguishable from those of carcinoma of the head of the pancreas. However, if the lesion is in the hepatic duct, the enlargement of the gallbladder which occurs in carcinoma of the pancreas or common duct is almost certain to be absent.

III. *Carcinoma of the Ampulla of Vater.*—Carcinoma of the ampulla of Vater deserves special consideration. Although many of the symptoms are the same as those occurring in carcinoma of the pancreas, or main biliary channels, there are certain noteworthy differences to which Cooper [12] has called attention: (1) pain is frequently an early symptom, (2) occult blood in the stools and secondary anemia are relatively constant observations and (3) roentgenologic changes in the second portion of the duodenum are frequently recognizable.

The surgical treatment of carcinoma of the ampulla offers a somewhat better prognosis than does that for carcinoma of the main biliary ducts and head of the pancreas. It is more accessible for resection, and Cooper [12] recorded metastasis in only about 20 per cent of the cases reviewed.

TABLE 4.—*Thymol Turbidity*

(Normal Value: 0.1 to 5.0 Units)

	No. of Cases	Range of Values	Average Value
Acute hepatitis	17	1.0 to 25.5	13.3
Cirrhosis	17	1.1 to 16.9	6.8
Acute cholangitis	2	2.3 & 5.3	3.8
Carcinoma of pancreas	6	0.6 to 7.8	3.5
Carcinoma of ampulla of Vater	0	.....	...
Carcinoma of common or hepatic duct	1	0.5	0.5
Carcinoma of liver	6	1.5 to 16.7	7.4
Stone in common or hepatic duct	20	0.9 to 19.6	4.3

IV. *Carcinoma of the Liver.*—Carcinoma of the liver may be primary but is more often metastatic. When primary it often develops on a cirrhotic basis, a fact which may cause some confusion in the interpretation of laboratory data. Jaundice is caused mainly by encroachment of the tumor on the biliary passages but may be caused also by damage to liver cells through interference with their circulation.

V. *Stone in the Common or Hepatic Biliary Ducts.*—Calculous obstruction of the main biliary passages, usually the common duct, ordinarily follows a history of cholecystic disease with repeated attacks of the characteristic severe pain which radiates to the back or scapular region, is associated with nausea and vomiting and is followed by tenderness in the gallbladder region and often by transient jaundice.

When evidence of biliary obstruction follows such a history, the laboratory data may be expected to conform to the clinical observations and the diagnosis early in the disease is not difficult. As a rule the obstruction is not complete; the serum bilirubin level, though elevated, is not excessively high, and secondary changes in the liver are not appreciable. However, if the obstruction is complete, or nearly so, and persists over a long period of time, the liver cells suffer from back pressure of the bile, there is interference with their blood supply and they may undergo atrophy. The obstruction which at first was simple becomes complicated by parenchymal changes in the liver, and one no longer is dealing with a simple disease. The disease may be further altered by the presence of infection with the development of cholangitis. In reaching a diagnosis in such a case the clinical history is likely to prove more valuable than results obtained from laboratory studies which are sensitive to the pathologic complexities of the condition.

TABLE 5.—*Cholesterol and Cholesterol Esters*

(Normal Values: Cholesterol, 150 to 300 Mg., and Esters, 105 to 210 Mg., per Hundred Cubic Centimeters)

	No. of Cases		Range of Values		Av. Value	
	Chol.	Chol. Esters	Chol.	Chol. Esters	Chol.	Chol. Esters
Acute hepatitis	29	21	135 to 283	53 to 219	202	113
Cirrhosis	23	19	91 to 903	13 to 222	240	118
Acute cholangitis	3	1	142 to 383	128	251	128
Carcinoma of pancreas	14	10	118 to 312	46 to 249	255	168
Carcinoma of ampulla of Vater	2	1	202 & 227	118	215	118
Carcinoma of common or hepatic duct	1	1	228	122	228	122
Carcinoma of liver	4	3	262 to 370	168 to 258	329	222
Stone in common or hepatic duct	13	9	153 to 600	93 to 167	261	124

The inclusion of stone in the common duct in a study of painless jaundice is justified because in a small percentage of such cases the jaundice caused by the calculous obstruction is not preceded or accompanied by pain. It is probable that in some cases pain or discomfort is experienced by the patient but is so slight that it is not interpreted as pain. In Zollinger's [10b] study of 75 cases of stone in the common duct, 91 per cent gave a history of biliary colic; presumably the remaining 9 per cent did not. In the 25 cases of common duct stone which I have reviewed there were 3 patients, 15 per cent, with common duct stone in which the history specifically stated that there was no pain.

TABLE 6.—*Serum Albumin and Globulin*

(Normal Values: Albumin, 4.6 to 6.7 Gm., and Globulin, 1.2 to 2.3 Gm. per Hundred Cubic Centimeters)

	No. of Cases		Range of Values		Average Value	
	Serum Albumin	Globulin	Serum Albumin	Globulin	Serum Albumin	Globulin
Acute hepatitis	39	39	2.9 to 6.0	1.4 to 4.7	4.3	2.6
Cirrhosis	34	34	1.8 to 5.1	1.1 to 7.0	3.3	3.4
Acute cholangitis	2	2	4.4 & 4.9	2.2 & 2.6	4.7	2.4
Carcinoma of pancreas	17	17	2.0 to 6.0	1.7 to 4.1	3.9	2.3
Carcinoma of ampulla of Vater	2	2	3.4 & 3.6	2.3 & 2.7	3.5	2.5
Carcinoma of common or hepatic duct	1	1	3.2	2.1	3.2	2.1
Carcinoma of liver	5	5	3.7 to 5.4	1.8 to 3.2	4.4	2.7
Stone in common or hepatic duct	11	11	2.8 to 6.4	1.6 to 3.6	4.4	2.4

It is in this type of case that laboratory methods of diagnosis are particularly useful. They are also of value

12. Cooper, W. A.: Carcinoma of the Ampulla of Vater, Ann. Surg. 106: 1009-1034 (Dec.) 1937.

in determining the extent of hepatic damage. In his work on strictures of the common bile duct Walters [13] found the degree of response of the prothrombin time of the blood to vitamin K and the amount of serum globulin and its relation to the serum albumin the most practical indicator of the degree of injury to the liver.

TABLE 7.—*Alkaline Phosphatase*

(Normal Values: 2 to 3.5 Units)

	No. of Cases	Range of Values	Average Value
Acute hepatitis	32	2.3 to 13.6	7.4
Cirrhosis	30	2.7 to 34.8	9.0
Acute cholangitis	3	6.4 to 14.4	10.1
Carcinoma of pancreas	18	7.4 to 24.4	14.3
Carcinoma of ampulla of Vater	1	14.8	14.8
Carcinoma of common or hepatic duct	2	14.1 & 18.6	16.3
Carcinoma of liver	3	8.7 to 16.5	12.6
Stone in common or hepatic duct	21	4.4 to 31.0	12.2

VI. *Cirrhosis of the Liver.*—Jaundice occurring in chronic hepatitis (cirrhosis) is a late manifestation of the disease and is not, as a rule, pronounced. By the time clinical jaundice appears, a diagnosis of cirrhosis is likely to have been already established. Cirrhotic jaundice probably is of mixed regurgitation and retention types due to cicatricial constriction of the cholangioles and to cellular damage caused by cicatricial interference with blood supply. Extrahepatic obstruction occasionally occurs when pancreatitis is associated with the cirrhosis. The serum protein usually shows a relative increase in globulin with a decrease in albumin. The cephalin-cholesterol flocculation test of Hanger [14] as a rule is positive, and there is often sulfobromophthalein sodium retention. The differentiation to be made is mainly between cirrhosis of the liver and carcinoma. Final diagnosis may depend on peritoneoscopy or biopsy, though both procedures involve some risk to the patient.

COMMENT

The bile, or icterus, index and the serum bilirubin determinations as shown in tables 1 and 2 have no real specificity, but the degree of jaundice has some diagnostic significance, particularly in the obstructive lesions of the extrahepatic ducts. Obstruction due to cancer of the ducts or the head of the pancreas ordinarily gives a higher value than obstruction due to stone. Cancer of the ampulla of Vater, however, gives a relatively low reading because the obstruction is prevented from becoming complete by the constant breaking down of the tumor. The icterus index in the parenchymatous diseases of the liver depends largely on the stage of the disease at which the determination is made and shows variations too wide to be of any great diagnostic value.

The particular value of the cephalin-cholesterol flocculation test of Hanger [14] (table 3) is in the differentiation of the parenchymatous from the obstructive types of jaundice. In acute hepatitis, for example, the Hanger reaction is likely to be strongly positive early in the disease, whereas in the obstructive lesions the reaction is at first negative or mildly positive and becomes more strongly positive only after the liver cells have been injured.

The results of the thymol turbidity test of Maclagen [15] (table 4) closely parallel those of the Hanger test. The reaction in acute hepatitis is strongly positive, but in the presence of obstructive lesions it is likely to be normal or nearly so.

In acute infectious hepatitis and other parenchymatous diseases of the liver there is generally a reduction of cholesterol and its esters in the blood (table 5). In the obstruction group of lesions, however, the cholesterol content of the blood is increased. The changes in these small groups of cases do not appear particularly striking.

TABLE 8.—*Average Values Obtained in Jaundice-Producing Disease*

Normal Values:	Icterus Index, 4 to 6 Units	Serum Bilirubin, 0.2 to 0.8 Mg. per 100 Cc.	Hangar Test, Negative	Thymol Turbidity, 0.1 to 5.0 Units	Cholesterol and Cholesterol Esters: Cholesterol...150 to 300 Esters.....105 to 210 Mg. per 100 Cc.		Serum Albumin and Globulin: Albumin.....4.6 to 6.7 Globulin.....1.2 to 2.3 Mg. per 100 Cc.		Alkaline Phosphatase, 2.0 to 3.5 Units
					Cholesterol	Esters	Serum Albumin	Globulin	
Acute hepatitis	80.7	8.1	3.4+	13.3	202	113	4.3	2.6	7.4
Cirrhosis	48.6	3.1	2.5+	6.8	240	118	3.3	3.4	9.0
Acute cholangitis	40.3	7.4	Neg.	3.8	251	128	4.7	2.4	10.1
Carcinoma of pancreas	90.1	9.2	0.7+	3.5	255	168	3.9	2.3	14.3
Carcinoma of ampulla of Vater	45.5	...	3+	...	215	118	3.5	2.5	14.8
Carcinoma of common or hepatic duct	161.0	...	Neg.	0.5	228	122	3.2	2.1	16.3
Carcinoma of liver	48.2	7.8	1.7+	7.4	329	222	4.4	2.7	12.6
Stone in common or hepatic duct	44.8	7.4	1+	4.3	261	124	4.4	2.4	12.2

Determination of the ratio of serum albumin to globulin has its principal value in the differential diagnosis of cirrhosis of the liver. In this disease the value of the globulin fraction approaches and often exceeds that of the albumin fraction (table 6).

The determination of alkaline serum phosphatase has its principal usefulness in distinguishing jaundice due to injury of hepatic cells from that caused by obstructive conditions. In table 7 it will be observed that the average values in the nonobstructive or hepatocellular diseases is below 10 Bodansky units, whereas in the obstructive conditions the average values are above 10.

The normal values given in the tables apply specifically to the laboratory of St. Luke's Hospital. In certain cases the results of laboratory tests do not conform closely to those which are expected in the particular disease, but average values are fairly consistent. Not all of the laboratory data are tabulated, but results are shown for the tests most widely employed.

13. Walters, W.: Physiologic Studies in Cases of Stricture of the Common Bile Duct, read at the meeting of the American Surgical Association, April 20-22, 1949.

14. Hanger, F. M.: Serological Differentiation of Obstructive from Hepatogenous Jaundice by Flocculation of Cephalin-Cholesterol Emulsions, J. Clin. Investigation **18**: 261-269 (May) 1939.

15. Maclagen, N. F.: Thymol Turbidity Test: New Indicator of Liver Dysfunction, Brit. J. Exper. Path. **25**: 234-241 (Dec.) 1944.

Highly reliable results can be obtained, as Robinson and Moyer [16] have demonstrated, by a series of relatively simple laboratory tests that can be performed in almost any hospital with basic equipment.

SUMMARY

The diseases that give rise to jaundice are almost invariably associated at some stage with a certain amount of pain. The term painless jaundice is therefore used in a relative sense.

Jaundice directly concerned with the liver and biliary passages is divided into two main types, retention jaundice and regurgitation jaundice. In retention jaundice the hepatic cells are affected and jaundice develops because the cells are unable to perform their normal excretory function. In regurgitation jaundice the cells are active; however, because of obstruction in the extrahepatic biliary ducts or in the cholangioles within the liver, the products of excretion are prevented from reaching the intestinal tract and the bile which has been excreted is eventually regurgitated into the blood.

Certain laboratory procedures have been demonstrated to be of value in the differentiation of the two types of jaundice.

The principal diseases underlying the development of jaundice and the means of their differentiation have been discussed.

Accurate diagnosis of the disease which is responsible for painless jaundice often depends on the use of all possible aids, both clinical and laboratory.

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PERIODIC DISEASE

Periodic Fever, Periodic Abdominalgia, Cyclic Neutropenia, Intermittent Arthralgia, Angioneurotic Edema, Anaphylactoid Purpura and Periodic Paralysis

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There are a number of disorders which recur with remarkably regular periodicity over many years without affecting the general health otherwise. In different persons the episodes are characterized by different features, which allow an arrangement of the disorders accordingly into four groups as periodic fever, periodic abdominalgia (benign paroxysmal peritonitis), periodic (cyclic) neutropenia and periodic (intermittent) arthralgia.[1] The name periodic disease was proposed to embrace the conditions in a newly established symptom-complex, but it appears that periodicity of disease was known to the ancients and was ascribed to the influence of solar and lunar cycles.[2] Knowledge of its cause has not progressed much further. Infectious, allergic, endocrinologic, epileptic or migrainous influences have been held responsible; however, as Mead [3] wrote apropos of the subject in 1704, "and thus far the foundation was good, but when a false theory happened to be joined to true observation, this did considerably puzzle the affair."

The object of this paper is to report the subsequent course and further study of cases discussed in a previous article,[1] to describe new cases, to cite reports of cases published by others or furnished in personal communications from physicians and to suggest the inclusion of certain forms of so-called anaphylactoid purpura, angioneurotic edema and perhaps of periodic paralysis among the periodic conditions.

PREVIOUSLY REPORTED CASES

PERIODIC FEVER

CASE 1.—Mrs. N. W., aged 50, whose attacks began in 1936 when she was 37, continues to have periods of chills, fever, nausea and pain in the abdomen, chest and extremities; these last five to seven days and recur every 17 to 22 days in no relation to a normal menstrual cycle. Because of reports by Cooke [4] and Rowe [5] of patients with similar conditions who were relieved of symptoms by withdrawal of certain foods, further studies were directed toward the discovery that some offending protein was the possible cause of the condition. However, a rigid "elimination diet" consisting of lamb, rice, tea, salt and sugar followed for three weeks had no effect on a current episode. The discomfort of so restricted a diet precluded further trial. The patient also spent a month a long distance from her home, likewise without effect on the symptoms. The excretion of porphyrin in the urine was measured in eleven samples collected during four weeks by Dr. Cecil Watson, but all determinations were in the normal range without evidence of fluctuation.

CASE 2.—S. L., a man continues to have weekly episodes of fever and abdominal pain which began in 1938. He was restudied after the report of Gross [6] that regular recurrences of chronic malaria were ended by the injection of testosterone, on the assumption that a cyclic endocrinologic disturbance was the cause. In July 1948 the gonadotropins measured less than 6 international units and the estrogens, 24 mouse units. Testosterone propionate, 50 mg., was then injected intramuscularly twice a week for four weeks, but without effect on the episodes of the patient and without significant changes in the amount of excreted gonadotropins, estrogens or 17-ketosteroids.

Because of a statement in his prior history that relief from the episodes persisted for six months during a period of involuntary restriction of diet, the same elimination diet as that prescribed in case 1 was applied for two weeks. Nonetheless, the regular episode occurred.

Finally, since Moore [7] had described several instance of what he regarded as abdominal epilepsy in which anticonvulsive drugs gave relief, this possibility was considered. However, an electroencephalogram was interpreted as normal and anticonvulsive therapy was not employed.

CASE 3.—E. H., a physician, still has attacks of abdominal pain, fever and leukocytosis at intervals of one week to one month. His condition may be regarded as either periodic fever or abdominalgia.

CASE 4.—L. F. has had cyclic neutropenia and ulcers in his mouth at twenty-one day intervals since 1945. Further studies were made and are reported elsewhere.[8]

CASE 5.—Mrs. C. B. continues to have episodes of arthralgia of the same joints at intervals of fourteen days, which began in 1944.

CASE 6.—A. P., with recurrent myasthenia, died from pneumonia.

16. Robinson, J. R., and Moyer, C. A.: Methods for Differential Diagnosis of Painless Jaundice, Surg. Gynec & Obst. **85**: 535-540 (Oct.) 1947.

From Jefferson Medical College and Hospital.
Read before the Section on Internal Medicine at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1949.

1. Reimann, H. A.: Periodic Fever: A Probable Syndrome Including Periodic Fever, Benign Paroxysmal Peritonitis, Cyclic Neutropenia and Intermittent Arthralgia, J. A. M. A. **136**: 239-244 (Jan. 24) 1948.

2. Periodic Disease, editorial, Lancet **1**: 565-566 (April 10) 1948. de Rudder, B.: Über Sogenannte "Kosmische" Rhythmen beim Menschen, Leipzig, Georg Thieme Verlag, 1937, pp. 1-45. Kleitman, N.: Biological Rhythms and Cydes, Physiol. Rev. **29**: 1-30 (Jan.) 1949.

3. Mead, R., cited in editorial.[2]

4. Cooke, R. A.: Gastrointestinal Manifestation of Allergy, Bull. New York Acad. Med. **9**: 15-24 (Jan.) 1933.

5. Rowe, A. H.: Fever Due to Food Allergy, Ann. Allergy **6**: 252-259 (May-June) 1948.

6. Gross, S. J.: Male Hormones for the Prevention of Relapses in Malaria, Indian M. Gaz. **82**: 65-66, 1947.

7. Moore, M. T.: Abdominal Epilepsy, Rev. Gastroent. **15**: 381-389 (May) 1948; Paroxysmal Abdominal Pain: A Form of Focal Symptomatic Epilepsy, J. A. M. A. **124**: 561-563 (Feb. 26) 1944.

8. Reimann, H. A., and de Beradinis, C. T.: Periodic (Cyclic) Neutropenia: An Entity; A Collection of Sixteen Cases, to be published.

REPORT OF NEW CASES

PERIODIC FEVER

CASE 7.—H. D., a Negro aged 42, complained of attacks of fever, weakness and headaches. In May 1947 he had a chill, nausea, headache and fever which kept him in bed four or five days. Attacks thereafter occurred about every six weeks, later at approximately four week intervals. When the episodes became severer in January 1948, he entered the hospital for study.

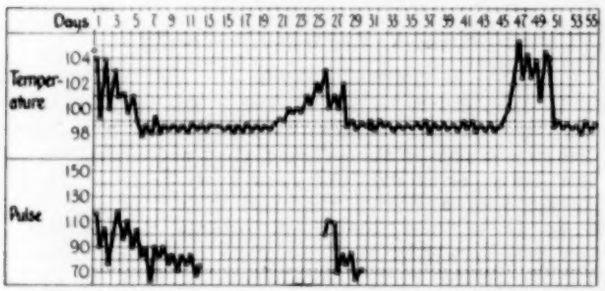

Fig. 1 (case 7).—Episodes of fever with tachycardia recurring every twenty-three days. Record of the pulse rate was made during observation in the hospital.

Physical examination revealed a muscular Negro suffering with an attack of severe chills. His temperature was 40 C. (104 F.), and the pulse rate was 120 (fig. 1). The scleras and pharynx were injected, but no other abnormalities were detected. Examination of the blood did not disclose anemia or sickling. The leukocytes numbered 5,000 and 6,000 with normally distributed component cells. The sedimentation rate by the Cutler method was 21 mm. in sixty minutes. Plasmodia were not found, and reactions to the Wassermann test, cold agglutination test, tuberculin and histoplasmin skin tests and liver functional tests were negative. Roentgenograms of the thorax and long bones revealed essentially normal conditions. The clinical impressions were brucellosis, miliary tuberculosis, Hodgkin's disease or other lymphoma.

The temperature returned to normal, as it had after previous episodes, and the patient left the hospital in apparently good health. He was again admitted three weeks later for an attack of similar nature and with similar negative observations (fig. 1).

At a third admission to the hospital in June, twenty-four days after the preceding one, he appeared to be severely ill, with coughing, temperature of 40.5 C. (105 F.), tachycardia (150) and complaints chiefly of weakness and pains in his calves (fig. 2). The severity and duration of attacks, which now lasted about ten days, increased. Except for rales in the bases of both lungs, all studies were again without significant results. The leukocytes numbered 5,400; the urine contained albumin (3 plus); a blood culture was sterile, and roentgenography did not reveal intrathoracic abnormality. Ten days later, when the temperature was normal, the leukocytes numbered 3,000; a van den Bergh test gave a positive direct result, 18 per cent of sulfobromophthalein sodium was retained and the serum bilirubin measured 1 mg. per hundred cubic centimeters. The proteins of the blood were normal in amount. The cells of the sternal marrow were normal, and no abnormal lymph nodes were palpable. Administration of aminopyrine in doses of 0.60 Gm. reduced the temperature of the patient to normal on two occasions.

The urinary gonadotropins were less than 6 international units, the estrogens 12 mouse units and the 17-ketosteroids 12.9 mg. per hundred cubic centimeters. He then was given testosterone propionate 50 mg. three times a week intramuscularly for three weeks without effect on the episodes. Under observation, the episodes recurred at 25, 22 and 27 day intervals. He left the hospital in good health and returned to work as a chauffeur.

An attack began twenty-eight days after the preceding one had started. He went to another hospital with fever (40.5 C., 105 F.), for which penicillin was given without effect. On his transfer to Jefferson Medical College Hospital, his temperature was elevated (fig. 2). He appeared to be severely ill but significant abnormalities were not found on examination or in laboratory studies. After ten days of fever aminopyrine therapy again brought the temperature to normal. After recovery, the 17-ketosteroids measured 26 mg. per hundred cubic centimeters. There was no evidence of endocrinologic dysfunction. The patient became well again, but he died suddenly during the next episode in August in another city. Unfortunately, further information is not available.

CASE 8.—E. F., a youth aged 17, had had hay fever for ten years, and several members of his family had allergic disturbances. In May 1947 red swellings 2 to 3 cm. in diameter appeared transiently over his body and face, occasionally accompanied with redness and swelling of his phalangeal joints. These attacks disappeared in November 1947. In October 1947 an attack of fever (40 C., 104 F.) had occurred, lasting an hour and causing profuse sweating, dull frontal headache and stiffness of his arms and legs for twenty-four hours. The patient was well until another cycle recurred in fourteen days. Thereafter the episodes took place at two week intervals, and the headache became worse. During one attack a shaking chill was noted.

The patient was hospitalized in June 1948 (fig. 3). Two days later a predicted episode occurred, but examination revealed no other abnormalities except warmth and tachycardia (130). An excised axillary lymph node showed chronic lymphadenitis. The leukocytes before the episode numbered 5,400 with 64 per cent polymorphonuclear cells; during fever there were 11,800 cells with 98 per cent neutrophils, and after the episode there were 4,600 cells, with 43 per cent neutrophils. The sedimentation rate by the Cutler method was 15 mm. in thirty-five minutes. Three blood cultures were sterile. There were no agglutinins for Brucella, and the heterophil antibody test gave a normal result. Plasmodia were not seen. The cells of the sternal marrow were normal. Roentgenograms of the thorax and spine revealed no abnormalities. After two similar episodes, the number of leukocytes fell to 4,800 and 2,900, respectively. A tuberculin test caused no reaction. The basal metabolic rate was —8 per cent during an episode and —20 and —33 per cent in fever-free periods. Six units of crystalline insulin given intravenously caused mild hyopglycemic symptoms in fifteen minutes, without other evidence of endocrine dysfunction. Endocrinologic studies revealed the following: urinary gonadotropins less than 6 international units; estrogens less than 12 mouse units; 17-ketosteroids 2.4 mg. per hundred cubic centimeters; on July 9 gonadotropins were 39 units, estrogens 44 units and 17-ketosteroids 6.6 mg. After these tests were made testosterone propionate 50 mg. was

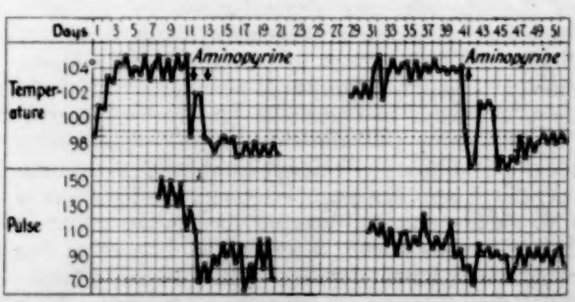

Fig. 2 (case 7).—Later episodes of longer duration and greater severity, observed in the hospital. Aminopyrine was antipyretic. Death occurred in the next episode.

given to the patient intramuscularly twice a week until September 10 (two months). Six days after the first injection the gonadotropins measured less than 6 units, the estrogens 64 units and the 17-ketosteroids 5.7 mg. The episodes (fig. 3) came at intervals of 10, 9, 7, 9, 7, 8, 8 and 12 days. After the patient left the hospital (at the point where the pulse rate curve stops in figure 3) he recorded his temperature at home. The height of the fever declined, the bouts were shorter and the symptoms were milder. This improvement was coincident with testosterone therapy, but it is doubtful whether it was caused by the drug.

He returned to the hospital September 7. No changes were evident on examination or in the laboratory data. The leukocyte count varied from 3,700 to 4,300 cells. When last heard from in January 1949 he had worked without interruption but had bouts of stiffness of his arms and body and low grade fever "every two or three weeks." The temperature chart which was prepared at home shows four days of fever (37.5 C., 99.5 F.) at 8, 6 and 8 day intervals.

CASE 9.—Mrs. R. C., aged 50, had menopausal symptoms several months after hysterectomy and oophorectomy were performed in 1944. In June 1945 a shaking chill occurred, lasting thirty minutes. The next week headache began. It started in the evening and was followed by a chilly sensation during the night and temperature which often reached 40 C. (104 F.). The episode lasted twenty-four hours and was followed by a period of relative comfort for twenty-four hours, after which another attack began. This cycle recurred regularly every other day. She entered a hospital for a three week period of observation. Because of the short cycles of high fever and chilliness, malaria was suspected but not proved. Quinine, quinacrine hydrochloride, sulfanilamide and penicillin were given without effect on the febrile periods. The attacks persisted, causing a loss of 22 pounds (10 Kg.) in four months.

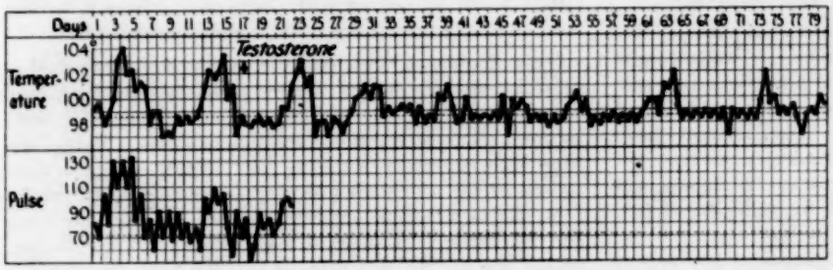

Fig. 3 (case 8).—Episodes at seven to twelve day intervals. The degrees of fever were less after testosterone therapy was begun, but the temperature, after recording of the pulse rate ceases, was measured at home.

In February 1946 therapy with estrogens was begun and continued for a year. The febrile episodes gradually lengthened to three to four day intervals, as illustrated in figure 4. They were not as severe as before but lasted forty-eight hours. She improved somewhat after some of the menopausal symptoms disappeared. In 1947 a physician suspected quartan malaria because of the four day cycles of fever and administered in turn pamaquine naphthoate, quinacrine hydrochloride and quinine, again without effect. The cycles gradually lengthened to seven days. Because of the appearance of abdominal pains at irregular intervals in no relation to the febrile episodes or to food, and because of roentgenologic evidence of gallstones, the gallbladder was removed in February 1948. During her convalescence the febrile episodes were milder, recurring about every seven days; later they became as severe as before. Antipyretic drugs provided transient relief. She felt well between the episodes.

The patient came under my observation in 1948. The febrile episodes were her only complaints except nervousness and occasional aching in the fingers and shoulders. There was no evidence of allergy or other disturbance in the woman or her family.

Examination during an interval or during an episode revealed a healthy looking woman. No significant abnormalities were discovered. All routine laboratory studies made in a hospital in 1945 and at the time of writing gave normal results. The leukocytes during one episode numbered 11,500 with 56 per cent neutrophils, 41 per cent lymphocytes, 1 per cent monocytes and 2 per cent eosinophils; during an interval they numbered 6,500 and 4,300 with 28 per cent lymphocytes and 12 per cent monocytes. Plasmodia were not found. The sedimentation rate and blood protein determinations were normal. An electroencephalographic tracing was interpreted as normal.

The temperature registered at home for several weeks and under my observation for two weeks is illustrated in figure 5. Recurrences were not as regular as the patient had stated; the intervals varied from 3 to 9 days.

Between Dec. 8, 1948 and Jan. 14, 1949 temperature measurements at home showed periodic attacks of fever 6, 5, 7, 7, 5 and 5 days apart.

CASE 10.—(The record of this patient was placed at my disposal by Dr. Robert Loeb at Presbyterian Hospital, New York, who permitted me to publish an abstract of it. She was studied over thirty years in the medical wards on about twenty occasions, and she made many more interim visits to the outpatient department. To date she has had episodes almost without interruption for thirty-seven years. The diagnosis came to be regarded as "Tatosian's" disease after the patient's name.) Mrs. M. T. O., aged 40, at the age of 3 years had had pain in the abdomen, chills and fever, which occurred after she ingested a large meal and lasted a day. Thereafter similar attacks recurred at intervals of approximately two weeks. Her tonsils were removed without effect on the attacks.

She was first studied at the Presbyterian Hospital in 1918 at the age of 9 years, having had recurrent episodes for six years. An attack was characterized by chilliness, fever (up to 40 C., 104 F.) and pain in the abdomen; it lasted twenty-four to forty-eight hours and was succeeded by a period of good health which persisted until the next episode. Leukocytosis occurred during the episodes, with one count of 37,000. A physician suspected malaria. Her appendix was removed because of suspected chronic appendicitis at a different hospital without effect on the recurrences.

Although the episodes were said to have occurred at two week intervals, a three week hospital record in February 1921 listed three bouts of fever 5, 4 and 8 days apart. Reaction to a Wassermann test at this time was positive. Syphilis, miliary tuberculosis, Hodgkin's disease, lymphosarcoma and focal infection were considered as diagnoses. In April 1923, the cervical lymph nodes were swollen and the patient jerked and twitched in a manner suggestive of chorea or hysteria. A second tonsillectomy was performed, again without effect on the episodes. Soon afterward, both shoulders and one knee hurt during the febrile bouts and the leukocytes numbered 13,000 to 15,000. Reaction to another Wassermann test was negative. Because itching of the conjunctivas preceded some attacks and there was some swelling over the ankles, angioneurotic edema and a possible allergic basis were suspected. All of the usually applied skin tests for protein gave negative results. The episodes during that period of study came at six day intervals.

On different occasions during the following years the patient was given elimination diets, rice diets, wheat-free and milk-free diets, was kept in a room with filtered air and was denied cosmetics, all without effect, yet an impression persisted that some allergic disturbance was a fault. There was never eosinophilia; there were no other allergic manifestations and no history of allergy in her relatives. Temperature charts over several periods recorded in the hospital showed febrile episodes at intervals of 5, 4, 7, 8, 6 and 7 days in 1927; 3, 3, 2 and 3 days in 1930; 10, 20, 16, 4, 20 and 9 days in 1931, and 5, 4, 6 and 35 days in 1936. In spite of this record, episodes at home were said to recur about every two weeks, and oftener when she was "run down" or agitated. Occasionally they were spaced at exactly seven days. She was free from episodes for one three-month period and in several shorter ones.

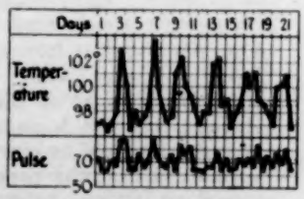

Fig. 4 (case 9). — Episodes at three and four day intervals in 1946.

Throughout the years of study, innumerable laboratory studies and roentgenograms were made and many consultations were held without fruitful results. During observation she had several severe infections of the respiratory tract and

fractures; she was given quinine, arsenicals, sulfonamide drugs and other forms of therapy. In May 1942 cholecystectomy revealed a normal gallbladder with a few stones, but there were peritoneal adhesions and free peritoneal fluid suggested a chronic form of peritonitis. No episodes occurred during the last seven months of a normal pregnancy in 1945, and the patient stated that she "never felt better" in her life.

At the time of writing, 1949, episodes recur sometimes once every other month and sometimes twice a month. They are of two kinds, one with a chill, fever and abdominal pain, the other with arthralgia and temperature of 40 C. (104 F.).

Case 11.—(The record of this patient was supplied by Dr. Marion M. Young of Pleasant Hill, Tenn.) A woman aged 68 had had episodes of fever, malaise and arthralgia for over twenty years. Malaria was suspected but never proved, and antimalarial therapy was of no avail. The episodes have recurred always at regular intervals, at first every twenty-eight days and now every fourteen days. Fever (to 39 C., 102 F.) lasts two or three days and is reduced by salicylate drugs. Laboratory data are not available.

Case 12.—Mr. T. W., aged 54, was a patient of Dr. Myron Prinzmetal of Beverly Hills, Calif., who permitted me to use the data. The first febrile episodes occurred three or four times a year in 1941. They consisted of severe chills lasting an hour followed by temperature of 39.5 C. (103 F.), severe sweating and complete recovery after twelve or fifteen hours. During the next few years the episodes came at shorter intervals. Malaria was suspected, but Plasmodia were not found and quinine had no effect. All laboratory studies gave negative results, and physical examination disclosed no abnor-

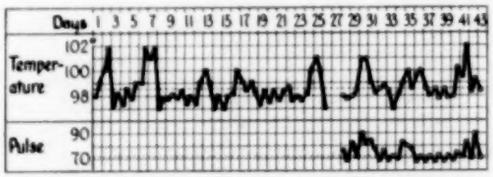

Fig. 5 (case 9).—Episodes at three to eight day intervals recorded at home until the twenty-sixth day, then in the hospital in 1948.

malities. Intensive treatment with penicillin, sulfonamide drugs and streptomycin gave no relief.

By 1946 the attacks increased in severity and the duration to thirty-six to seventy-two hours. Malaria was suspected again, but chlorguanide hydrochloride had no effect. At the time of writing attacks are said to be still more frequent, coming at approximately 7 to 10 day intervals. A tracing made from temperature registered by the patient Feb. 25 to April 5, 1948, shows intervals of 20, 14 and 9 days from the beginning of one episode to the start of the next. Sometimes the episodes begin without chills, but fever, headache and perspiration are constant and last five or six days, so that there are few days between attacks on which the patient feels well.

Case 13.—P. K. (a patient of Dr. W. C. Mumler of Los Angeles) has had bouts of fever for five years. They have been characterized by pharyngeal injection, backache, headache, generalized muscular pains, fever (up to 39 C., 102 F.) and severe prostration lasting six or seven days; they have occurred regularly at intervals of six or eight weeks. The leukocytes have numbered from 8,000 to 10,000. The spleen has been palpable during each attack since 1946. All studies including those for malaria have revealed essentially normal conditions. In May 1947 an attack seemed to be terminated by penicillin therapy and there was no recurrence until May 1948.

Case 14.—D. W., a man aged 28, was seen by Dr. Howard Alt of Chicago (who permitted the use of this record, and who will report the case with others in detail elsewhere). The patient had had episodes of chills and fever since the age of 10 months. They recurred during his childhood at six weeks to two month intervals and lasted three days to two weeks, requiring rest in bed. He was well between times. There were no other symptoms. For the past five years the attacks came every six months. An observed episode occurred at a hospital in February 1947. On admission the patient had shaking chills, a temperature of 41 C. (105 F.) and tachycardia (120). There were no other abnormal observations except a faint systolic murmur. Endocarditis or typhoid was suspected, but all laboratory studies gave normal results. The leukocytes numbered 7,000, and Plasmodia were not found. The patient had several more chills and temperature of 40 C. (104 F.), but he recovered the next day; however, he had one more chill and fever (39 C., 102 F.) on the fourth day.

Case 15.—Brick [9] reported the case of a man aged 41 whose periodic episodes began twelve years ago in 1937, with an attack of fever, chills and myalgia. Between 1937 and 1943 episodes recurred three or four times a year. Since 1946 they have recurred every three to four weeks. They are characterized by the symptoms previously mentioned and by drenching perspiration, headache, anorexia, nausea (occasionally vomiting) and temperature of 40 to 40.5 C. (104 to 105 F.) lasting four to six days. He was studied sixteen times at one hospital, where many tests were made; sulfonamide compounds, antibiotics and transfusions of blood were given; tonsillectomy, exploratory laparotomy and appendectomy were performed, all without effect on the episodes.

In one episode observed by Brick, the temperature rose to 40.3 C. (104.6 F.) and the spleen became palpable. Results of all examinations were normal, except for leukopenia—3,000 cells with 28 per cent neutrophils. The number of eosinophils fell from 122 before to zero during the episode. Plasmodia were not observed and the patient was given a course of quinacrine hydrochloride without effect. The next episode began twenty-one days after the beginning of the one observed.

Although the following case is grouped with those of periodic fever, the patient had symptoms and signs different from the rest, characterized by involvement of the upper part of the respiratory tract, dermal eruptions, diarrhea, stiffness of the muscles, stupor and signs of disturbance of the central nervous system. The episodes caused severe illness.

Case 16.—The case of a white boy aged 13 was submitted to the editor of *Arizona Medicine* [10] for analysis. The child had had about eighty attacks of severe illness since the age of 2 years. The episodes came every six to eight weeks in the winter and every two to four months in the summer, each lasting seven to ten days. The onset always began with symptoms of an acute infection of the respiratory tract; in infancy the episode was of that nature alone. Later fever (40 C., 104 F.), drowsiness or stupor, polydipsia, polyuria, an erythema-multiforme-like or urticarial rash, diarrhea, enlarged cervical lymph nodes, pneumonia and muscular stiffness recurred in varying combinations. The boy has been well between times. His mother and two cousins have allergic disorders.

During one observed episode which lasted eleven days, the temperature reached 40 C. (104 F.), the pharynx was inflamed, cervical adenopathy was present, the boy was somnolent and an urticaria-like eruption appeared on the extremities. Pathologic great toe reflex and Kernig's sign were present bilaterally. There were rales and blood-streaked sputum. The spleen was felt once. There were no abnormalities of the cranial nerves. The patient recovered abruptly from the attack. The next episode began forty-one days after the start of the one described. The leukocytes numbered 18,600. The stools were passed involuntarily and sometimes contained blood. Blood cultures were sterile; agglutination tests, roentgenograms of the chest

9. Brick, I. B.: Periodic Disease: A Case of Intermittent Fever, Splenomegaly and Leukopenia of Eleven Years' Duration, Bull. Georgetown Univ. M. Center (April-May) 1949.

10. Arizona Medical Problems: Consultation and Case Analysis, Case no. 5, Arizona Med. 5: 81-85 (Jan.) 1948.

and the spinal fluid examination gave normal results. During the next four months only one attack occurred, which was said to have been aborted by an injection of plasma and isotonic solution of sodium chloride.

Studies at another hospital in 1948, when the patient was 16 years of age, were unrevealing except for an electroencephalogram which was interpreted as consistent with an epileptic disease. The diagnosis was recorded as "Friedreich's ataxia (?), retinitis pigmentosa." Periodic angioneurotic edema affecting the central nervous system may be a better suggestion.

PERIODIC (CYCLIC) NEUTROPENIA

In the previous paper,[1] case 4 was described together with 3 cases of periodic (cyclic) neutropenia reported in the literature. Since then the records of 12 other cases, most of them reported after 1946, have been gathered and described elsewhere.[8] Certain features of cases in this group are of interest, especially the remarkable regularity of the three week interval and the similarity of signs and symptoms in all 16 cases. In 1 instance there were recurrences for thirty-four years. In another, episodes were grouped over three periods only. Arthralgia was noted in 3 instances and abdominal pain in 1. Genetic relationship was evident in 1 case. Concurrent thrombopenia and purpura were observed in another. Eosinophilia was reported in 3. Splenectomy caused lessening of or relief from symptoms in 4 patients, but periods of neutropenia of lesser degree persisted. Splenectomy gave no relief in 2 cases.

PERIODIC (INTERMITTENT) ARTHRALGIA

CASE 17.—(This record was furnished by Dr. Joseph Stokes Jr.). M. E. P., a woman aged 54, had pain in her right knee at the age of 17 after a bruise, but roentgenography and removal of a piece of cartilage were without effect. Since then pain, heat and swelling have recurred in both knees, chiefly in the right one, at twelve to thirteen day intervals for thirty-seven years. At the age of 35 stiffness was noted at times simultaneously in her fingers and elbows, similar to the circumstances in case 5. In 1919, 1928 and 1940 attacks ceased for about six months. There was no relation of the episodes to the menstrual cycle, and they persisted after hysterectomy was performed in 1940.

Dr. Marian W. Ropes of Boston informed me of 5 of her patients. One had hydroarthrosis in both knees at six day intervals. In the second both knees were affected at twelve and sixteen day intervals for seven years. In the third, one knee was involved every ten days, in another an elbow was swollen every ten days; and in the fifth case, one knee was affected regularly every twenty-eight days.

In a query[11] sent to the editor of a medical journal, diagnostic aid was sought for a woman aged 26 who had low grade fever, stiffness, discomfort and swelling of the fingers, hands and arms and general malaise regularly "every few weeks" for three years. The leukocytes during an episode numbered 9,000 with 8 per cent eosinophils. All other studies were negative. From the paucity of data available, the patient may have had either periodic arthralgia with fever, which is unusual, or periodic fever with arthralgia.

PERIODIC ABDOMINALGIA (BENIGN PAROXYSMAL PERITONITIS)

Cases 1, 2, 3 and 10, which are grouped as periodic fever, also involved abdominal pain and may be included also under the heading of periodic abdominalgia (benign paroxysmal peritonitis). Because there was no evidence of actual peritonitis in these cases or in case 19, they as well as some reported by Siegal[12] and others here may be designated more appropriately by the broader term periodic abdominalgia; visceralgia may be a better name, because pain in the chest, extremities and elsewhere is a usual accompaniment. Heberden[12a] refers to "pains which are regularly intermittent, the fits of which return as periodically as those of an ague; such I have known in the bowels, stomach, breast, loins, arms and hips, though it be but seldom that these parts suffer in this manner." Laparotomy in 3 of Siegal's patients during attacks revealed widespread edema of the peritoneum in one, moderate vascular injection in another and congestion of the entire abdominal contents of a third. These changes would seem to be compatible with a vasomotor disturbance similar to that causing urticaria or angioneurotic edema.

CASE 18.—H. C., a Jewish salesman aged 29, was referred for study by Dr. T. H. Mendell. The patient had his first attack of chills, perspiration, fever, leukocytosis and pain in the right lower part of the abdomen in 1944. Thereafter attacks came at irregular intervals with good health between. Episodes as recorded by the patient came at 34, 14, 36, 40, 59, 24 and 14 day intervals. Some attacks did not interfere with his work; others have required rest in bed. He was studied in numerous hospitals, on one occasion in 1946 for a bleeding duodenal ulcer. Innumerable laboratory and other tests, save for leukocytosis, revealed normal conditions. Malaria was suspected, but Plasmodia never were found. Penicillin and streptomycin therapy were ineffective.

Study of the patient during an episode revealed fever (38.5 C., 101 F.), pulse rate of 98, tenderness in the right lower quadrant of the abdomen with moderate rigidity of the right rectus muscle. The patient walked bent to the right. The leukocytes numbered 21,000, with 85 per cent polymorphonuclear cells and 2 per cent eosinophils. The sedimentation rate by the Cutler method was 15 mm. in sixty minutes. Recovery was prompt.

CASE 19.—S. C., a Jewish student aged 20, at the age of 5 years had had a severe sore throat followed by swelling of his extremities thought to be angioneurotic edema from allergy. Similar edema recurred at the age of 6 years after a gastrointestinal disturbance. At the age of 11 years, attacks of "upset stomach" and severe abdominal pain began to recur once a month, gradually increasing in frequency to once every thirteen to fifteen days. Two or three days before an episode there is erythema of the arms and chest which persists during the incident. Edema of the feet and aching immediately precede nausea, vomiting, diarrhea and severe pain either in the right lower quadrant of the abdomen or in the epigastrium. There is no fever, leukocytosis or eosinophilia. The episodes last three to four days. The patient was given a strict elimination diet for six weeks, but episodes recurred as usual. In some episodes external evidence of angioneurotic edema predominates, in others it is minimal and abdominal distress is dominant. During one of the severe abdominal attacks, a roentgenogram made after ingestion of a barium meal by the patient showed an "irritative" pattern of the small intestine with mucosal edema, segmentation and hypermotility. There was no diarrhea. Evidence points to a vasomotor disturbance, not peritonitis, as a cause.

Dr. Robert Loeb called my attention to several similar patients studied in his service and permitted the following abstracts to be made.

CASE 20.—Mr. G. H., aged 19, has had weekly attacks of fever (40 C., 104 F.) and abdominal pain since the age of 3.

11. Polyarthritis, Queries and Minor Notes, J. A. M. A. **139**: 192 (Jan. 15) 1948.

12. (*a*) Siegal, S.: Benign Paroxysmal Peritonitis, Ann. Int. Med. **23**: 1-21 (July) 1945; (*b*) Benign Paroxysmal Peritonitis: Second Series, Gastroenterology **12**: 234-247 (Feb.) 1949.

12a. Heberden, W.: Commentaries on History and Care of Diseases, London, Ch. 29, p. 151, 1806.

In January 1947 he had generalized urticaria, but all allergic tests gave negative results. Appendectomy gave no relief.

CASE 21.—Mr. M. G., aged 55, had attacks of fever and abdominal pain lasting a day every two to three months for twenty-seven years. Pain often began in the shoulders or hips and spread to the abdomen.

CASE 22.—Mr. M. K., a Jewish salesman aged 34, had pain in the right side of his chest and abdomen and fever lasting a day or two for seventeen years. At first the episodes occurred every three weeks, at present every ten days. Appendectomy gave no relief. The leukocytes were sometimes normal in number and at other times increased to 15,000 during the bouts. Periodic abdominal pain and fever occur in three of his brothers.

PERIODIC PARALYSIS

The syndrome of periodic paralysis, because of its striking characteristics, was one of the first periodic conditions to be studied. In many reports cited in Talbot's review,[13] one as early as 1687, attacks came at weekly intervals for years. Many instances of multiple cases in families are recorded. An association of the episodes of paralysis with change in the distribution of potassium often occurs, but whether the change is a cause or an effect is unknown. However, in most cases no mention is made of angioneurotic phenomena, fever, pains or changes in the leukocyte count characteristic of other periodic disorders.

PERIODIC (ANAPHYLACTOID) PURPURA AND PERIODIC (ANGIONEUROTIC) EDEMA

It is probable that certain cases of so-called anaphylactoid purpura (Schönlein-Henoch syndrome) and angioneurotic edema belong to the group of periodic disorders under discussion. The patient and his brother with fever and abdominal pain described by Alt and Barker[14] were subsequently regarded as having Henoch's purpura by Althausen, Deamer and Kerr.[15] In cases 10, 16, 19 and 20 of this report, urticaria and/or angioneurotic edema were prominent features. Except for the absence of purpura, case 10 could be regarded as typical of Schönlein-Henoch's syndrome and case 19 of Henoch's syndrome. Anaphylactoid purpura according to most textbook descriptions is said to be recurrent, but little attention was given to determining any regularity of cycles. In Osler's[16] series of cases, several patients were reported as having episodes at intervals of a week to a month for many years; in 1 for fifty-four years. According to Wintrobe,[17] episodes of several days' duration occur with intervals of eight days or more, and Minot[18] has stated that recurrences come at one to six week intervals. Many authors suspect that allergy plays a role, and in a few cases removal of an offending protein from the diet of the patient stopped recurrences. However, it is generally admitted that the cause is unknown.

In Osler's[19] report of hereditary angioneurotic edema in five generations of a family, several members were recorded as having recurrent attacks at regular intervals for many years. In a man aged 92, episodes had recurred at intervals of a month or six weeks for seventy-four years. Osler cited reports of other authors in which "there was a remarkable regularity in the sequence of attacks which recurred on the seventh, fourteenth or twelfth days." Whitfield[19a] described the case of a woman, aged 39, who had edema of the ankles for a few days about twelve times a year for twenty-two years. There is little doubt, therefore, that certain cases of both anaphylactic purpura and angioneurotic edema, which Osler regarded as related conditions, can be included among the periodic diseases.

COMMENT

The disorders grouped as periodic disease can be placed into more than the four categories first suggested.[1] In addition to periodic fever, periodic abdominalgia, periodic neutropenia and periodic arthralgia, it is likely that the cyclic thrombopenia of Demmer,[20] certain forms of so-called anaphylactoid purpura, angioneurotic edema and familial periodic paralysis belong to the group. Perhaps others such as Behcet's syndrome[21] also may be included. From the descriptions given, it seems that certain instances of Kahlmeter's allergic rheumatism,[22] Solis-Cohen's[23] angioneural arthroses and Hench's[24] palindromic rheumatism represent cases of periodic arthralgia, an opinion shared by Weber.[25] A query[26] to the editor of a medical journal describes periodic pain in the extremities affecting sixteen members in five generations of a family. The trouble starts in infancy and continues throughout life. Pain in the extremities lasts one or two days and recurs at intervals of a few days to a few weeks. These and the conditions described herein may be unrelated entities, but they are more likely to be different manifestations of the same cyclic underlying cause. If so, for the sake of simplicity, it would seem preferable to name them with the adjective "periodic" before each descriptive term and to group them as follows:

Periodic Disease

Periodic fever	Periodic purpura
Periodic abdominalgia	Periodic thrombopenia
Periodic arthralgia	Periodic edema or urticaria
Periodic neutropenia	Periodic paralysis (?)

A unity is suggested by the similar duration of the cycles in each and by overlapping symptoms and signs. For example, the differentiation of periodic fever with abdominal pain from periodic abdominalgia with fever is an arbitrary one. Leukopenia or arthralgia are present in several cases of periodic fever. In many instances of periodic abdominalgia there is arthralgia, and in periodic neutropenia there is at times arthralgia.

13. Talbot, J. H.: Periodic Paralysis: A Clinical Syndrome, Medicine **20**: 85-143, 1941.
14. Alt, H. L., and Barker, M. H.: Fever of Unknown Origin, J. A. M. A. **94**: 1457-1461 (May 10) 1930.
15. Althausen, T. L.; Deamer, N. C., and Kerr, W. J.: The False "Acute Abdomen": II. Henoch's Purpura and Abdominal Allergy, Ann. Surg. **106**: 242-251, 1937.
16. Osler, W.: The Visceral Lesions of Purpura and Allied Conditions, Brit. M. J. **1**: 517-525 (March 7) 1914.
17. Wintrobe, M. M.: Clinical Hematology, Philadelphia, Lea & Febiger, 1942, p. 577.
18. Minot, G., in Cecil, R. L.: Textbook of Medicine, Philadelphia, W. B. Saunders & Company, ed. 7, p. 1100.
19. Osler, W.: Hereditary Angio-Neurotic Edema, Am. J. M. Sc. **95**: 362-367, 1888.
19a. Whitfield, A. G. W., and Armott, W. M.: Chronic and Unexplained Oedema, Lancet, **2**: 225-228 (Aug. 6) 1949.
20. Demmer, T.: Morbus Maculosis Werlhofii in Regelmässigen vierwochentlichen Schuben bei einem 60-jährigen Mann nebst Untersuchungen über Blutplättchen, Folia haemat. **26**: 74-86, 1920-1921.
21. Katzenellenbogen, I.: Recurrent Aphthous Ulceration of Oral Mucous Membrane and Genitals Associated with Recurrent Hypopyon and Iritis (Behcet's Syndrome): Report of Three Cases, Brit. J. Dermat. & Syph. **58**: 161-172, 1946.
22. Kahlmeter, G. Y.: A-t-il des formes de rheumatisme et périarticulaire d'une nature reellement allergique? Acta. med. Scandinav. **102**: 432-443, 1939.
23. Solis-Cohen, S.: On Some Angioneural Arthroses (Periarthroses, Parathroses) Commonly Mistaken for Gout or Rheumatism, Am. J. M. Sc. **147**: 228-243 (Feb.) 1914.
24. Hench, P. S., and Rosenberg, E. F.: Palindromic Rheumatism, Arch. Int. Med. **73**: 293-321 (April) 1944.
25. Weber, F. P.: Palindromic Rheumatism, Lancet **2**: 931-932 (Dec. 29) 1946.
26. Familial Periodic Pain, Queries and Minor Notes, J. A. M. A. **139**: 1123 (April 16) 1949.

abdominal pain or fever. Urticaria and angioneurotic edema occur in conditions called periodic fever, abdominalgia ar intermittent arthrosis [26a]; but these manifestations also are characteristic of the Schönlein-Henoch syndrome in which there occur abdominal pain and/or arthralgia, with or without purpura. Except for periodicity, in periodic paralysis there are apparently none of the features of the other diseases.

Most striking are the regular predictable recurrences of the episodes with uniform characteristics for years, in 2 instances (cases 10 and 17) for thirty-seven years and in Osler's case seventy-four years, usually without otherwise affecting the general health. Of particular interest is the regular rhythm of about three weeks in all 16 cases of periodic neutropenia. In most instances the episodes persist, when once established.

Of the 53 cases of periodic disease described or cited here and previously, 36 were in males and 17 in females. Except in periodic paralysis, most victims are ambulatory during their episodes; however, in 2 patients (cases 7 and 16) the attacks were severe, and death from an unknown cause occurred during one episode (case 7). Death occurs occasionally from edema of the glottis in periodic edema, from infection in periodic neutropenia and from several causes in periodic purpura.

The onset of periodic illness of so many persons in infancy suggests a congenital basis. Heredity is shown in instances in which similar disturbances existed in siblings (Siegal,[12] Alt and Barker [14] and case 22) and in parents.[27] Osler and others record many familial groups with purpura and edema, and heredity is obvious in many cases of periodic paralysis. The manifestations may not become clinically apparent until late in life. Siegal [12b] has pointed out that all his patients with abdominalgia were either Jewish or Armenian. Three of the 5 patients with abdominalgia reported herein were Jewish, but no such ethnic predominance occurs in the other periodic diseases.

CAUSE OF PERIODIC DISEASE

The cause of periodic disease is unknown, but several theories have been proposed involving infections, allergy, endocrinologic or nervous influences, or some connection with known or unknown intrinsic or extrinsic cycles.

Infections.—It would be most unlikely for any known infection to cause regularly recurrent relapses of similar intensity and character for many years without some pathognomonic evidence, or recovery or deterioration and death of the victim. In all instances of periodic fever, infection was sought and empiric treatment was without avail. Rheumatic fever, tuberculosis and brucellosis often were considered, but in most instances malaria was suspected. In no case have Plasmodia been found, and antimalarial treatment has had no influence on the episodes. Surgical operations performed to remove supposed sources of infection have never given relief.

In this connection the observations of Putnam, Boyd and Mead [28] are of interest. They have reported cycles of parasitemia regularly recurrent at twelve to sixteen day intervals in several patients in the late stage of malaria due to Plasmodium vivax. The recurrences were believed to be attributable either to unknown aspects of the parasitic cycle or to intermittent activity of the host's mechanism of defense. Male patients with chronic malaria as observed by Gross [6] had recurrences at regular three to four week intervals, which led him to suspect the influence of some inapparent menstrual-like cycle, as discussed in a later paragraph.

Allergy.—Features characteristic of allergic disturbance are present in many of the patients described or in their genetic relatives. Furthermore, in the patients of Cooke [4] and Rowe [5] and in others with anaphylactoid purpura, episodes ceased after an offending food protein was deleted. Yet in spite of repeated attempts in some cases reported here and elsewhere,[12] tests for specific hypersensitivity to proteins were unrevealing and severely restricted diets failed to alter the periodic symptoms. It is still possible, of course, that some undisclosed specific hypersensitivity to unknown agents accounts for periodic disease, but, as in the case of infections, it is difficult to believe that such hypersensitivity could cause clinical episodes so uniform and so regularly recurrent for decades. Furthermore, causes other than hypersensitivity to protein provoke urticaria, angioneurotic edema, eosinophilia or other evidence of vasomotor dysfunction. Except perhaps for periodic neutropenia, a vasomotor disturbance could indeed account for most of the signs or symptoms in the various forms of periodic disease. But even if it did, the reason for its regular recurrence still would be a mystery.

Endocrinologic Disturbance.—The regular rhythmic recurrence of the menstrual cycle suggested to some observers its association with some of the periodic disorders in question, as discussed previously.[1] It was suggested that perhaps a similar undetected cycle was present in men to account for some periodic conditions in that sex. Studies by others,[29] however, showed a constant excretion of androgenic and gonadotropic substances in a number of normal men with no hint of rhythm. In many instances the onset of the disorders began in infancy when sexual hormonal cycles are unlikely to occur. In no cases in women were the disorders synchronous with menstruation; they may begin after the menopause or in men over 60 years of age.

In cases 4, 7 and 8 no abnormalities were detected in the excretion of estrogens, gonadotropins or 17-ketosteroids, and the administration of diethylstilbestrol or testosterone had no influence on the episodes in cases 1, 2 and 7. In case 8 the episodes as recorded were less severe after therapy with testosterone propionate, but the change may have been coincidental. Fluctuations in the excretion of 17-ketosteroids in synchrony with cyclic neutropenia was noted in 1 instance [30] and large amounts of gonadotropins were excreted in another,[31] but similar changes were not detected in case 4. In none of my patients was there clinical evidence of any endocrine disturbance.

26a. Kahlmeter,[22] Solis-Cohn,[23] Weber,[25] Berger, H.: Intermittent Hydrarthrosis with an Allergic Basis, J. A. M. A. **112**: 2402-2405, 1939.

27. Siegel,[12] Wolf, S., and Wolff, H. G.: Intermittent Fever of Unknown Origin: Recurrent Fever with Benign Outcome in a Patient with Migraine and Notes on Neurogenic Fever, Arch. Int. Med. **70**: 293-302 (Aug.) 1942. Vahlquist, B.: Cyclic Agranulocytosis: Report of a Case with Short Survey of the Disease, Acta. med. Scandinav. (supp.) **170**: 531-542, 1946.

28. Putnam, P.; Boyd, M. F., and Mead, P. A.: Periodic or Cyclically Recurring Phenomena of Vivax Malaria Infection, Am. J. Hyg. **46**: 212-214, 1947.

29. Pederson-Bjergaard, K., and Tønnesen, M.: Sex Hormone Analysis Acta. med. Scandinav. (supp. 213) **131**: 284-297, 1948.

30. Reznikoff, P.: Cyclic Neutropenia: A Case Study with Bone Marrow Findings Before and After Splenectomy, Tr. A. Am. Physicians **59**: 276-281, 1946.

31. Rolland, C. F.: Personal communication to the author.

Ask-Upmark [32] presented 2 cases of hyperparathyroidism with recurrent fever, 1 with episodes at seven day intervals which were abolished by excision of the glands. In 1 patient with hyperparathyroidism studied at this hospital over a three month period, three episodes of low grade fever appear on the temperature chart at intervals of 21, 36 and 25 days. Studies pertinent in this respect were reported by Richter and his associates.[33] Regular periods of activity were caused in rats after the endocrine system was disturbed by the removal of various endocrine glands. Extirpation of one gland supposedly released a cycle caused by another, thus upsetting a pattern and establishing a rhythm not evident in the normally functioning animal. For examples, a thirty-four day cycle was observed in a parathyroidectomized monkey and in a patient with hypoparathyroidism; a fourteen day cycle appeared after the pituitary stalk was divided in rats and a twenty-five to thirty-five day cycle after thyroidectomy. Whether or not these observations have any bearing on the problem cannot be decided at present.

Migraine and Epilepsy.—A possible relation of periodic disorders to migraine was suspected in a patient of Wolf and Wolff.[27] Under the heading abdominal epilepsy, Moore [7] has reported relief in 3 patients by the administration of diphenylhydantoin sodium and phenobarbital. One was a woman aged 50 in whom seizures of abdominal pain recurred every other day. The second patient, a boy 12 years of age, had abdominal pain every ten days. He also had hay fever and asthma. The third patient, aged 32, had recurrent abdominal pain since the age of 9 months with episodes every seven to eight days. Urticaria was present. The encephalograms of all 3 patients showed slight abnormalities. An abnormal electroencephalogram was also obtained in case 16. The matter is further complicated by evidence suggestive of both epilepsy and allergic disturbances in case 16 and in the patients of Moore just mentioned. Electroencephalograms made in cases 1, 2 and 9 showed no abnormalities, and therapy with diphenylhydantoin sodium failed to alter the episodes in case 1. No evidence of epilepsy or migraine was detected in any of my patients.

Biologic Rhythm.—Attention was drawn [1] previously to the curious fact that in many instances of periodic disease, including some of those described by Osler [19] and Ask-Upmark,[32] the duration of the cycles was approximately seven or multiples of seven days. Allusion was made to a possible association with the seven day week as established in ancient times on an astrologic or religious basis, or possibly on the basis of a natural rhythm of human life.[33a] It was called the "biological week" by Ask-Upmark.[34] A rhythm may be characteristic of mankind in general but inapparent except for its manifestations in extreme form in persons with periodic disease, in which the cycles cause disturbances great enough to attract attention. An alternate explanation [35] proposes that the human race has accustomed itself to the rhythm of the arbitrarily apportioned week and reacts in synchrony with it, which still leaves unanswered the question why the week was made of seven days in the first place. Against these views is the irregularity of episodes at times. In some victims the rhythm established early in life remains constant and predictable for decades; in others the episodes were widely spaced at first and shortened gradually, and in two instances (cases 9 and 14) the episodes began in short cycles and gradually lengthened.

Many observers, notably Huntington [36] and Toynbee,[37] regard the whole history of life as a record of cycles. Hersey [38] in discussing periodicity of mood and ability stated the belief that rhythm is a fundamental law of nature. For the present, speculation as to the cause of periodic disease may well rest here.

SUMMARY

Over 50 cases of periodic disease including periodic fever, periodic abdominalgia, periodic neutropenia, periodic arthralgia and periodic thrombopenia have been collected. They, together with many other recorded cases of periodic arthralgia (intermittent hydrarthrosis), periodic purpura (Schönlein-Henoch syndrome), periodic (angioneurotic) edema, and periodic paralysis are tentatively grouped as periodic disease and probably have a common cause. A hereditary aspect is apparent in many instances. A vasomotor disturbance seems to be the most obvious cause of the various clinical phenomena, but the reason for its regular rhythm is unknown. Theories as to the influence of infections, allergy, endocrinologic or epileptic factors are inadequate. Until further knowledge is attained, it is simplest to regard periodic disease as a manifestation of a rhythm of life.

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ABSTRACT OF DISCUSSION

DR. WESLEY W. SPINK, Minneapolis: It is appropriate at this time for Dr. Reimann to emphasize that all that is febrile is not infectious. Since potent antibacterial agents are available for the treatment of infectious disease, there is constant temptation to administer one of these drugs to the patient with fever of unknown causation. Many physicians have seen patients with prolonged fever who were given the sulfonamide drugs and one or more antibiotics but who were found to have leukemia, lymphoblastoma, carcinoma or even thyrotoxicosis. A few simple laboratory tests often will demonstrate that a febrile patient is suffering from one of these diseases. Attention should be called to another feature of the constant use of chemotherapy: Patients with sepsis of known cause, as staphylococcic sepsis with bacteremia, may be treated successfully with penicillin and later, after an interval of weeks or months, will have low grade fever. One should always consider the possibility of a walled-off abscess which does not present localizing symptoms. I have observed this sequence of events with staphylococcic sepsis. And, finally, I should like to say one or two words about fever being due to chronic brucellosis. This problem has interested the group with which I am associated for a dozen years, and we have investigated several hundred patients. It is the unusual patient with active brucellosis who does not have fever. The physician often will say, "the patient is not febrile," but if one takes the temperature every four hours, one will find in the proved case that there is fever. This is not new. Hughes, in his monograph on "Mediterranean Fever," published in the last century, made

32. Ask-Upmark, E.: On Periodic Fever, Acta. med. Scandinav., 1938, pp. 1-93.
33. Richter, C. P.; Honeyman, W. M., and Hunter, H.: Behavior and Mood Cycles Apparently Related to Parathyroid Deficiency, J. Neurol. & Psych. **3**: 19-25, 1940.
33a. Petersen, W. F.: Man, Weather, and Sun, C. C. Thomas Co., Springfield, 1947.
34. Ask-Upmark, E.: Den Kvinnliga Genitalcykeln och några Invärtesmedicinska Sjukdomstillstånd, Svenska läk.-sällsk. förhandl. **9**: 1-11, 1945.
35. Kleitman, N.: Personal communication to the author.
36. Huntington, E.: Mainsprings of Civilization, New York, John Wiley & Sons, Inc., 1945, p. 484.
37. Toynbee, A. J.: The Study of History, New York, Oxford University Press, 1948.
38. Hersey, R.: Emotional Cycles of Man, J. Ment. Sc. **77**: 151-160, 1931.

the statement, after studying several hundred cases of melitensis infection on the Island of Malta, "If fever is not present, active disease is absent." Too often, the diagnosis of chronic brucellosis is made on the basis of an ill-defined illness and a positive skin reaction. We do not use the skin test in our clinic.

DR. HAROLD JEGHERS, Washington, D. C.: Cases of unexplained fever, prolonged or of irregular duration, are a common problem in almost every hospital. They are frequently difficult to diagnose, often unsatisfactory as to treatment, and represent a great expense to the patient in the numerous studies that have to be made. We have been impressed with how frequently such instances are considered as synonymous with infection and so treated. There are literally several dozen conditions which can produce fever but which are not infectious in origin, and if the diagnostic studies are pointed entirely in the direction of an infection, many treatable or curable conditions can be overlooked. For example, fever occurs with severe pernicious anemia, lymphomas and other blood dyscrasias, many removable neoplasms, and many other systemic diseases. Dr. Reimann has provided a great service in emphasizing today that there are a number of important causes of elevated temperature that are overlooked. He has brought out in particular two or three varieties that are certainly not commonly recognized. In the past several months at Georgetown University Hospital, studies have been made of a male patient aged 46 who had had periodic fever for eleven years. The attacks would recur at intervals of a month up to occasionally as long as three months. A typical attack would consist of onset with chill and temperature of 103 to 105 F. sustained over a three to five day period and associated with leukopenia. Some eosinophil counts were made which disclosed a drop from 150 to 180 per cubic millimeters of blood to zero during the attack. The man had demonstrable pathologic conditions, particularly palpable splenomegaly, which receded when the attack was over. Numerous studies were made before, during and after one of those episodes, without a conclusion concerning the etiologic agent. It has been impossible to influence these attacks in any way. Over a period of many years, this person has been studied for disease in the abdomen. He has had numerous forms of therapy, including some of the newer antibiotics such as aureomycin. Apparently there is a periodic condition of this nature, the cause of which is still unknown. Apparently, it is not infectious. I am sure that this paper by Dr. Reimann will bring many of these cases to light. A second patient recently has been brought to my attention, a man aged 24 who has not yet been studied in the hospital. His story is that of recurrent ulcers in the mouth, periodic abdominal pain and a mild fever which has occurred with "the regularity of a menstrual cycle" (as he put it) once a month for the last five years. If they are looked for, I am certain that many more of these cases of periodic fever will be found.

Mona Lisa.—Leonardo Da Vinci (1451-1519), sculptor, artist, architect, scientist, poet and musician, was the illegitimate son of a notary. He, too, realized the importance of studying the cadaver, for it is recorded that he dissected over 30 bodies of old and young people by candle-light in the mortuary of Santo Spirito in Rome. To him perhaps we owe the aphorism "we are as old as our arteries," for he relates how he dissected the blood vessels of an old man of 100 and then those of a child of 2, comparing and portraying them. He held that every motion was expressed by every fiber of the body and therefore every muscle should be known by the artist. The best example of this dictumis, of course, is his picture of Mona Lisa, which is said to depict the exquisite play of 36 muscles of the face. Therefore, should any of you feel interest, it would well repay you to visit Windsor Castle, where a great number of his drawings of the human frame were bought and brought by William Harvey at the bequest of our King Charles I.—V. B. Green-Armytage, M.D., The Debt of the Fine Arts to Medicine, *Cambridge University Medical Society Magazine*, Easter term, 1949, Reprinted from "The Embryo," Summer, 1947.

TREATMENT OF SHIGELLA ENTERITIS WITH ORAL STREPTOMYCIN

A Report of Thirty-Four Cases

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Several preliminary reports have appeared in the literature indicating that shigellosis responds favorably to treatment with streptomycin. The National Research Council Committee [1] reported 2 cases of Shigella-caused dysentery in which a daily dosage of 1.5 Gm. of streptomycin was given intramuscularly for five days. In both cases, the stool cultures promptly became negative and an uneventful recovery ensued. Pulaski and Amspacher [2] treated 10 patients who had bacillary dysentery due to Shigella with streptomycin in doses of 1 to 4 Gm. daily for periods ranging from one to twelve days. The drug was administered orally in 2 cases, parenterally in 6 and in combination in 2. These investigators reported good to excellent results in nearly every case, with no instances of relapse during a one to four month follow-up period.

In view of the toxic reactions observed in connection with parenterally administered streptomycin, it was considered worth while in a series of cases of enteritis caused by Shigella organisms to use orally administered streptomycin exclusively. Toward this end, a diarrhea ward was set up at Children's Hospital in the summer of 1947, and all patients admitted to the hospital with the complaint of diarrhea were admitted directly to this ward. Three consecutive daily stool cultures were obtained on all patients, and, in those cases in which the Shigella organism was isolated, oral streptomycin therapy was started without delay. Thus, during 1947 and 1948, in 34 cases of Shigella enteritis, infants and children ranging in age from 3 months to 12 years were treated with orally administered streptomycin. For purposes of comparison, 20 additional patients with bacillary dysentery were treated with sulfadiazine, while 16 were managed with aerosporin (polymyxin B).

METHODS AND MATERIALS

Of the 34 patients, 25 were admitted in the acute phase of the disease, while 9 were carriers. At least two positive cultures were obtained in each case prior to the institution of therapy. During treatment, stool cultures were obtained daily until the patients were discharged from the hospital. The mediums used included Salmonella-Shigella (SS) agar, desoxycholate citrate agar and tetrathionate broth. The rectal swab technic was routinely employed, and all stools were seeded simultaneously on these three mediums. Over four hundred stool cultures were obtained in this series (an average of twelve per patient). It may be well to

Miss Sara Stevens and Mrs. Susan Gougé gave technical assistance.
From the Research Foundation of Children's Hospital, Washington, D. C. and the pediatric services of the Georgetown and George Washington University Schools of Medicine.
This study was supported by a grant from the Antibiotic Study Section of the Division of Research Grants and Fellowships, The National Institutes of Health, United States Public Health Service.

1. Streptomycin in Treatment of Infections: Report of One Thousand Cases, National Research Council, Committee on Therapeutics and Other Agents, J. A. M. A. **132**: 4 (Sept. 7); 70 (Sept. 14) 1946.
2. Pulaski, E. J., and Amspacher, W. H.: Streptomycin Therapy for Certain Infections of Intestinal Origin, New England J. Med. **237**: 419, 1947.

point out that the Salmonella-Shigella agar proved to be the most sensitive medium in the isolation of shigellae, while Kauffman's tetrathionate broth was the least useful. On the other hand, for the isolation of salmonellae from stools, tetrathionate broth is considerably more effective in our experience than either the Salmonella-Shigella agar or the desoxycholate citrate agar.[3]

It should be emphasized that with the use of these three mediums in combination the chances of detecting growth of either shigellae or salmonellae on stool cultures are extremely good. In this series, 15 infectious cases were identified as caused by organisms of the Flexner group, while the other 19 were caused by the Sonne type of bacilli.

DOSAGE AND DURATION OF THERAPY

Arbitrarily, during the initial phase of this study, 100 to 200 mg. of streptomycin were administered orally every four hours. However, it was soon found that larger doses were required to sterilize the bowel of its pathogenic organisms in the active cases. We subsequently decided that 400 mg. every four hours (2.4 Gm. per day) was a more efficacious dose. This latter dosage was used both in the active cases and in the carrier group. It is our impression that perhaps a smaller dose (200 mg. every four hours) might be sufficient to clear up infections in the carrier group adequately; however, in acute cases the larger dose of 400 mg. every four hours seems to be required, in view of the more precipitous passage of stool flux through the intestinal tract during the acute phase. No intramuscularly administered streptomycin was used in this series.

The duration of treatment with orally administered streptomycin ranged from 7 to 19 days with an average of 10.7 days per patient. The total dose varied from 8.4 to 57.6 Gm., the average being 24.4 Gm. per patient. The drug was well tolerated, and toxic reactions were not observed. All the patients, including the infant age group, accepted the orally administered streptomycin well.[4]

RESULTS

In all 34 patients in this series, rapid disappearance of the Shigella organism from the stool occurred shortly after therapy was started. Daily stool cultures made during the course of therapy permitted observation of the fact that disappearance of the Shigella organism occurred from one to four days after the start of treatment. The Sonne strains appeared to respond as promptly as the Flexner organisms.

In the 25 cases of acute shigellosis the number of positive stool cultures obtained after starting streptomycin treatment ranged from zero to four, with an average of 1.6 per patient. On the other hand, in the carrier group, none of the 9 patients showed positive stool cultures within twenty-four hours after institution of therapy. An average of ten negative stool cultures were obtained in each case before the patient was considered cured. Once the stool became negative, no cultural reversals were noted during the hospital stay.

In 5 of the acute cases, however, a recurrence of positive stool cultures was noted within one month after discharge of the patient from the hospital. This may have represented either a relapse or a reinfection. This latter possibility must be considered in view of the fact that many of the families, including the siblings and parents, were similarly infected with shigellosis. It was sometimes difficult to persuade the remaining members of these families to submit to treatment in spite of a demonstrable pathogen in the stool. Such was the case in the families of 4 of the 5 patients whose stool cultures showed a recurrence of Shigella organisms.

Clinically the improvement was commensurate with the salutary effect observed bacteriologically. In the acute cases a high elevation of temperature, pronounced drowsiness and frequent watery stools (many of which showed associated blood and mucus) were often noted at the time of admission. Within twelve to twenty-four hours after therapy was started the patients usually manifested considerable clinical improvement characterized by a rapid decrease of temperature, prompt reduction in the number of stools (usually within one to three days) and disappearance of blood and mucus from the feces. In only a few cases, particularly among the infant group, was extensive adjuvant fluid therapy required, because the diarrhea was checked rapidly with streptomycin. An uneventful recovery occurred in all 34 cases, except for the previously noted cultural reversal in 5 instances.

COMPARISON OF STREPTOMYCIN, SULFADIAZINE AND AEROSPORIN THERAPY

In view of the high degree of bactericidal specificity of both sulfadiazine and aerosporin (polymyxin B) against Shigella organisms, it was considered worth while to treat a series of patients affected by shigellosis of comparable age and severity with the same methods employing the two aforementioned drugs in alternation with streptomycin. Thus, during the summer of 1948 we employed aerosporin in 16 cases of acute bacillary dysentery and administered sulfadiazine in 20 others. As noted previously, of the 34 patients treated with streptomycin, 25 were considered to be in the acute phase, and this latter group will be discussed, for purposes of comparison, in connection with data on the groups who received sulfadiazine or aerosporin.

All 61 patients with acute shigellosis were managed in the same fashion, and each case was followed with daily stool cultures during the course of therapy.

Aerosporin was administered exclusively by the oral route in all 16 patients. The dose most commonly employed was 3 mg. per kilogram of body weight every four hours. The daily dose of aerosporin ranged from 18 to 60 mg. Duration of treatment varied from 7 to 15 days, with an average of 10.5 days per patient. The sensitivity of the organisms to the aerosporin varied from 0.02 to 0.08 micrograms per cubic centimeter.

In the group of 20 patients receiving sulfadiazine therapy, the drug was given in a dose ranging from 0.25 Gm. to 1 Gm. every four hours. The duration of therapy varied from 5 to 21 days, with an average of 11.1 days per patient.

As was previously noted, the duration of therapy in the group treated with streptomycin averaged 10.7 days per patient. The streptomycin sensitivity in this group ranged from 3 to 5 micrograms per cubic centimeter.

A comparison of the rapidity of disappearance of the pathogen from the stool in the three groups may be considered to have some value as a therapeutic index

3. Ross, S.; Burke, F. G.; Rice, E. C.; Bischoff, H. W., and Washington, J. A.: Streptomycin in the Treatment of Salmonella Enteritis in Infants, New England J. Med. **240**: 602, 1949.

4. The drug was supplied as syrup of streptomycin (50 mg. per cubic centimeter) by E. R. Squibb & Sons.

of the efficacy of each drug. As will be noted in the accompanying table, all three drugs produced a prompt disappearance of the Shigella organism 2 days or less after the initiation of therapy. This slight variation was not considered statistically significant.

In 2 cases in the aerosporin-treated group, daily stool cultures showed the continued presence of Shigella organisms. After an unsuccessful trial of seven days of treatment with aerosporin in both cases, this drug was discontinued and the oral administration of streptomycin was instituted. Within two days, the stools showed a prompt clearing of Shigella organisms and both patients made an uneventful recovery. In the sulfadiazine-treated group, 1 patient was given sulfadiazine for nine days. However, daily stool cultures remained persistently positive for Shigella organisms. Orally administered streptomycin was substituted for sulfadiazine, and ten consecutive cultures during the course of streptomycin therapy were consistently sterile.

None of the group treated with streptomycin showed a refractoriness to the drug during the hospital stay, and in no instance was it necessary to substitute any other therapeutic agent.

Thus from the results obtained in this study, one may conclude that all three drugs are quite effective in the treatment of Shigella-caused enteritis when

Comparison of Streptomycin, Sulfadiazine and Aerosporin Therapy in 61 Cases of Shigella Enteritis

	Strepto-mycin	Sulfa-diazine	Aerosporin
No. of acute cases	25	20	16
Av. duration of treatment (days)	10.7	11.1	10.5
No. positive stool cultures after treatment started (av.)	1.6	2.0	1.9

administered orally. In regard to the drug of choice in this infection, one would be justified in summarily dismissing aerosporin from further consideration in view of its toxicity. It would require a considerably larger series than ours, however, to categorically state that streptomycin is superior to sulfadiazine. However, oral administration of streptomycin could be used advantageously in patients with a sulfonamide-resistant strain of Shigella organisms as well as in those cases in which there exists a sensitivity to sulfonamide compounds. In this regard, one may take cognizance of the relatively higher incidence of shigellosis in military personnel, especially in the tropical areas, coupled with the frequent hazard of administering a sulfonamide drug to dehydrated patients. In these conditions there exists the possibility that orally administered streptomycin may be found to be of considerable use as a substitute drug in the treatment of Shigella enteritis.

SUMMARY

1. Thirty-four infants and children with enteritis caused by Shigella organisms were treated with orally administered streptomycin.

2. In both the acute cases and the carrier group, a prompt disappearance of the pathogen from the stool followed the initiation of streptomycin therapy in every case. Clinically, the improvement was commensurate with the salutary effect observed bacteriologically. In 5 patients a cultural reversal was observed on stool culture within one month after discharge from the hospital. These may have represented either a relapse or a reinfection.

3. Comparison of orally administered streptomycin, aerosporin and sulfadiazine in the treatment of 61 patients with bacillary dysentery caused by Shigella indicates that all three drugs are effective agents. However, in view of the toxicity of aerosporin, streptomycin and sulfadiazine are the drugs of choice.

ACUTE HEMOLYTIC ANEMIA DUE TO NAPHTHALENE POISONING

A Clinical and Experimental Study

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In 4 cases of fulminating hemolytic anemia in young children observed during a period of two years the ingestion of moth balls consisting of pure naphthalene ($C_{10}H_8$) was the sole apparent etiologic factor. Experimental studies in dogs confirmed the hemolytic action of naphthalene. Since moth balls are a common and easily accessible household article, generally believed to be harmless, and since the American literature seems to contain no previous reports of this kind, the cases are reported in detail.

REPORT OF CASES

CASE 1.—A. W., a Negro girl aged 2 years, was admitted to the Children's Hospital of Michigan with the chief complaint of passing wine-colored urine. She had been entirely well until four days prior to admission, at which time she had diarrhea and seemed generally ill. The next day she became lethargic and passed urine of greenish tinge. The following day she refused nearly all her food although she seemed more active than before. On the day before admission she became feverish and passed port wine-colored urine. She also complained of dysuria. When asked routine questions the informant denied that the child had ingested any poisons, chemicals or medicine. The following day, however, the child's father admitted on specific questioning that on the day of onset of symptoms he had removed from the child's mouth the remnants of a moth ball which had been sucked to a small size and that shortly afterward he had again found the child sucking on another moth ball.

The past history was noncontributory. There was no history of anemia or illnesses similar to that of the patient in the family.

Physical examination revealed a pale irritable child, who appeared feverish and acutely ill. There was no icterus of the scleras. The heart rate was rapid, and a loud blowing systolic murmur was heard over the pulmonic area. The liver and spleen were not palpable. The remainder of the examination revealed essentially normal conditions.

The urine was port wine in color and contained albumin (4 plus), 5 to 6 leukocytes per high power field and many granular casts but no red corpuscles. The result of the benzidine test for hemoglobin was strongly positive. Spectroscopic examination failed to disclose porphyrins. The hemoglobin concentration of the blood was 5.2 Gm. per hundred cubic centimeters. The hematocrit reading was 17 volumes per cent. Unfortunately, the results of the red blood cell count were lost. The reticulocyte count was 6.8 per cent. The white cell count was 19,700. Differential counts showed 59 per cent neutrophils, 34 per cent lymphocytes, 3 per cent monocytes, 3 per cent eosinophils and 1 per cent basophils. There were 6 normoblasts per hundred leukocytes. No sickling was demonstrable in wet preparation. In dried smears stained with Wright's stain the erythrocytes showed definite anisocytosis and microspherocytosis, polychromasia and fragmentation. In the fragmented cells the outline was irregular and jagged over part of the circumference; the

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hemoglobin was irregularly concentrated on one side, and in the remaining portion the structure was often barely visible and the contour faint (fig. 1).

A marrow aspiration disclosed a relative increase in leukopoiesis and a shift to the left in erythropoiesis.

Chemical examination of the blood showed no increase in methemoglobin or sulfhemoglobin. The oxyhemoglobin concentration of the plasma was 39.5 mg. per hundred cubic centimeters. The Mazzini test for syphilis gave a negative reaction. The blood urea nitrogen was 12.5 mg. and the serum bilirubin 1.76 mg. per hundred cubic centimeters. Throat cultures yielded a heavy growth of hemolytic streptococci, some colonies of pneumococci and Staphylococcus aureus.

The diagnosis on admission was acute hemolytic anemia and hemoglobinuria of undetermined cause. The patient was given multiple transfusions of compatible blood and received sodium bicarbonate and sodium lactate in an attempt to alkalinize the urine. She remained feverish for three days but on the third day became alert and began to eat. The urine continued to contain hemoglobin for two and one-half days and albumin and occasional casts for three days. Thereafter the urine was normal. The white blood cell count returned to normal within three days, and after that time nucleated red cells and fragmented cells and microspherocytes were no longer seen. The patient was discharged in good condition seven days after admission and remained in good health during the following year.

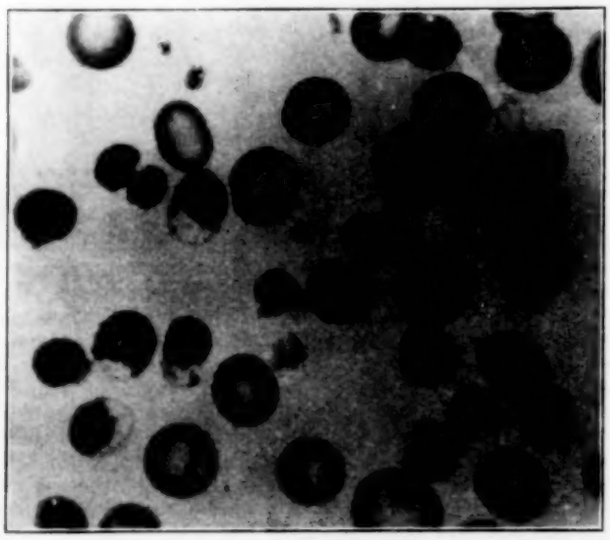

Fig. 1.—Blood smear, case 1. Note pronounced fragmentation of erythrocytes (Wright stain).

Urinalysis was supervised by Dr. Muehlberger, toxicologist for the Michigan Department of Health. A specimen obtained at the time of admission contained naphthol. A specimen collected the following day contained only a trace of naphthol, and all subsequent specimens were free of the compound, which is a derivative of naphthalene not found in normal urine.

The moth balls obtained from the parents consisted of commercial naphthalene.

Case 2.—H. S., a Negro boy aged 2 years, was admitted because of diarrhea of three days' duration. Earlier he had been entirely well. The stools had numbered six to eight daily, had been brownish green and watery, and had contained mucus. The child also became feverish, complained of nausea, vomited and refused to eat. On the second day of the illness the urine became red.

At the time of admission the temperature was 101 F. The child was pale (but not icteric), listless and acutely ill. The liver and spleen were not palpable. There was no sign of inflammatory disease of the respiratory tract.

The urine was port wine in color; it contained free hemoglobin and albumin but no red cells. Occasional leukocytes and granular casts were present.

The hemoglobin level of the blood was 4.2 Gm. per hundred cubic centimeters, the red blood cell count 1,780,000 and white cell count 25,000. The differential count was 58 per cent neutrophils and 42 per cent lymphocytes. There were 8 nucleated red cells per hundred leukocytes. The reticulocyte count was 10.8 per cent. There was no sickling of erythrocytes in wet preparations. The blood smear revealed the same features as those described in case 1, anisocytosis, microcytosis associated with spherocytosis, fragmentation of the red blood cells, polychromasia and, in addition, occasional Howell-Jolly bodies. Infrequent phagocytosis of erythrocytes by monocytes was seen.

The plasma oxyhemoglobin concentration was 54 mg. per hundred cubic centimeters. No increase in methemoglobin or sulfhemoglobin was demonstrable. The serum bilirubin level was 0.6 mg. per hundred cubic centimeters. Tests of the serum for cold hemolysins, autoagglutinins and isoagglutinins effective at various temperature in saline and albumin mediums were carried out with negative results.

Erythrocyte fragility was tested only by the "short" method of Straus and Faigin.[1] In 0.45 per cent saline solution there was 66 per cent hemolysis (normal less than 30 per cent). Reaction to the Mazzini test for syphilis was negative. The blood urea nitrogen was normal. The blood culture was sterile, and throat cultures yielded no pathogenic organisms. Marrow aspirations showed increased erythrogenesis.

The diagnosis on admission was acute hemolytic anemia and hemoglobinuria. On questioning the parents stated that one week prior to admission the child had sucked almost an entire moth ball and had probably ingested more moth balls during the following days. They had found two moth balls in the stool two days before admission. The course was somewhat more prolonged than that of the first patient but was otherwise similar. The response to blood transfusions and alkali therapy was favorable. Fever, lethargy, hemoglobinuria and albuminuria subsided gradually over a period of five days. Complete recovery ensued, and at the time of discharge results of the blood studies were within normal range.

Case 3.—L. B., a Negro boy age 2½ years, was admitted with the chief complaints of fever, sore throat and cough of three days' duration. The child had been entirely well until one week prior to admission, when he had coryza. A neighbor had seen him eating a moth ball four days before admission. On the same day he had become nauseated and had vomited. The mother administered a mixture of olive oil and liquid petrolatum in order to have the child vomit the moth ball, but the attempt was unsuccessful. The following day the child was feverish and complained of a sore throat. The fever persisted and swelling of the face, hands and feet was noted. The urine became dark red-brown two days before admission. The child had pain in the lumbar region and became pale.

In the past the patient had had numerous infections of the upper part of the respiratory tract as well as measles and whooping cough. The family history was noncontributory.

The patient was listless and appeared acutely ill. The scleras were slightly icteric. The mucous membranes were pale. The edge of the liver and the tip of the spleen were palpable. There was severe bilateral tenderness in the costovertebral angles.

Urinalysis showed albumin (3 plus), a trace of sugar, 3 to 4 red blood cells, 1 to 2 leukocytes and many granular casts. The result of the benzidine test was strongly positive. The urine was dark reddish brown.

Data on the blood are shown in table 1. The essential findings were the same as in cases 1 and 2. There was no sickling of the red cells, but fragmentation and spherocytosis were again noted. The plasma hemoglobin level was 38.0 mg. per hundred cubic centimeters. The icterus index was 64 units. However, hemoglobin and other pigments in the plasma probably interfered with accurate colorimetric readings. Blood urea nitrogen was within normal limits.

1. Straus, R., and Faigin, R.: Simplified Test for Fragility of Erythrocytes, Am. J. Clin. Path. **16**: 437, 1946.

The Donath Landsteiner test for cold hemolysins was negative, as were tests for atypical warm isoagglutinins or autoagglutinins. Cold agglutinins of a titer of 1:8 were present in the serum. The erythrocyte fragility was decidedly increased (96 per cent hemolysis in 0.45 per cent saline solution).

Therapy consisted of two blood transfusions and alkalinization. Within three days there was definite improvement. The urine became normal, and on the eleventh hospital day the child was discharged in good condition.

CASE 4.—D. T., a Negro boy aged 2 years and 3 months, was admitted because of listlessness and vomiting of three days' duration. On the day before the onset of these symptoms he had eaten the greater part of a moth ball. Subsequently he complained of abdominal pain and became exceedingly pale. The urine for a day became dark orange. The past history and family history were noncontributory.

Examination disclosed an extremely lethargic, irritable child who shortly afterward had a generalized convulsion. There was no icterus of the scleras. The tip of the spleen was palpable, and the liver descended 1 fingerbreadth below the right costal margin.

The urine was yellow and contained no abnormal elements other than a small amount of acetone. Examination of the blood disclosed severe anemia, normoblastemia, leukocytosis and reticulocytosis. The erythrocytes showed microcytosis, spherocytosis, fragmentation and an increased saline fragility. In a small number of erythrocytes Heinz bodies were seen in preparations stained with brilliant cresyl blue. There was also sickling of the majority of the cells. Because of this feature the blood of both parents was examined. Normal values were obtained in both, but the sickling trait was demonstrated in the father. The presence of the trait in only one of the parents seemed to indicate that the patient likewise had only the trait rather than sickle cell anemia.[2] This assumption was borne out by further observation and the return of red blood counts and reticulocyte counts to normal levels with recovery.

The Donath-Landsteiner test was negative, and neither isoagglutinins nor autoagglutinins were demonstrable. A cold agglutinin titer of 1:8 was obtained. The patient's cells gave a negative reaction to Coomb's test (detection of weak and incomplete Rh agglutinins).

The plasma hemoglobin was 13 mg. and the serum bilirubin was 0.78 mg., per hundred cubic centimeters. The blood urea nitrogen was in the normal range.

The patient received a single transfusion of 250 cc. of whole blood, which resulted in decided clinical improvement. The subsequent return of the blood values to normal is shown in figure 2.

EXPERIMENTAL DATA

Each of the cases represented an emergency at the time of admission, and it was therefore usually impossible to obtain serum for in vitro studies. Only in case 1 was a small amount of serum available. This material was diluted with isotonic sodium chloride solution and was incubated in a calibrated red-cell-counting pipet with whole blood from a normal donor of homologous type for three hours at 37 C. As a control, a corresponding dilution of normal homologous serum in the second donor was incubated with the same blood. Duplicate counts were made on each specimen. The count of the sample incubated with the patient's serum was 3,830,000; that of the control was 4,680,000. Both specimens were reincubated, but recount after a total of twelve hours of incubation revealed no further change. The result of this experiment, though suggestive, was not considered as conclusive evidence of an in vitro hemolytic effect of serum thought to contain absorbed naphthalene derivatives.

Naphthalene was given to 3 dogs (table 2). Varying amounts of pure naphthalene flakes were incorporated in the regular meat diet of the animals and were readily ingested. Preliminary determinations of hemoglobin, red blood cell count, hematocrit, reticulocytes, white blood cell count, serum bilirubin and, in 2 animals, erythrocyte fragility were made. Two of the dogs were in perfect health, the third was recovering from canine distemper which had caused moderate anemia. Since the blood values of this animal had shown stability over a five day period, it was believed that a decrease in these values after the ingestion of naphthalene would be significant.

Dog 1 received a total of 6.5 Gm. of naphthalene in divided doses during a five day period before any untoward symptoms were noted. On the fifth day the animal had diarrhea, the white blood count rose from a previous level between 13,500 and 15,000 to 25,500 and Heinz bodies suddenly appeared in the majority of the erythrocytes (fig. 3). On that day another 2 Gm. of naphthalene was given. The diarrhea persisted, the animal became lethargic and refused its food. A strong naphthalene odor of urine and stools was noted. On the seventh day the hemoglobin had fallen abruptly to a level of 5.6 Gm., the red blood count to 2,750,000 and the hematocrit to 20.5 volumes per cent; the Heinz body count had begun to drop, and the white blood count had risen to 32,000. Before these results were known the animal was given another 2 Gm. of naphthalene. Pronounced lethargy and ataxia were observed, and there was a further drop of the hemoglobin to 2.2 Gm. in the next three days. Fragmentation of erythrocytes, similar to that seen in the blood of the patients, was conspicuous. Simultaneously

TABLE 1.—*Hematologic Data of Patients on Admission*

Case	Hemoglobin	Red Blood Count	Hematocrit	Reticulocyte Count (%)	Nucleated Red Cells per Cmm.	White Blood Count	Fragmentation	Spherocytosis	Sickling	Erythrocyte Saline Fragility	Plasma Hemoglobin	Serum Bilirubin	Hemoglobinuria	Albuminuria	Urinary Sediment (per HPF)
1 (A. W.)	5.2	....	17	6.8	1,115	18,585	+	+	—	.....	39.5	1.76	+	+	Occ. WBC, many casts
2 (H. S.)	4.2	1.73	..	10.8	1,852	23,148	+	+	—	Increased *	54.0	0.06	+	+	Occ. WBC, many casts
3 (L. B.)	5.6	1.59	..	5.4	1,878	12,522	+	+	—	Increased *	38.0	?	+	+	Occ. WBC, RBC; many casts
4 (D. T.)	3.3	2.02	16	13.8	10,833	34,167	+	+	+	Increased	13.5	0.78	—	0	Rare RBC

* Short fragility method.

2. Neel, J. V.: The Genetics of Sickle Cell Anemia, to be published.

extreme leukocytosis (white blood count 119,000) developed. Reticulocytosis began on the eighth day and reached a maximum of 33.8 per cent on the twelfth day. The hemoglobin shortly began to rise, and eventually the animal made a complete recovery. By the eighteenth day the Heinz bodies had completely disappeared (fig. 4).

Dog 2 was given 3 Gm. of naphthalene in a single dose, an amount corresponding to the average weight of a moth ball. This was the animal with moderate anemia after an attack of distemper. The results of the experiment were similar in character and sequence to those in the first animal. On the second day Heinz bodies appeared in substantial numbers. On the third day the hemoglobin level began to fall, and by the eighth day a loss of approximately 3 Gm. per hundred cubic centimeters had occurred. There was severe leukocytosis during this period. Reticulocytosis had begun by the seventh day and reached a maximum of 19 per cent on the tenth day. Eventually all values returned to normal.

Dog 3 received an amount of naphthalene comparable to three moth balls in a single dose. Again lethargy, diarrhea and anorexia developed with the sequence of rapid rise in the number of Heinz bodies followed by a sharp drop in hemoglobin, fragmentation of red cells, leukocytosis and reticulocytosis. Eventual restoration of all blood values to normal levels ensued.

In each of the animals, an increase in the fragility of erythrocytes in hypotonic saline solutions was noted during the experiment and fragmentation of erythrocytes was evident in smears. The bilirubin concentrations of the plasma failed to rise significantly. In one of the animals transient albuminuria and slight microscopic hematuria were observed.

For in vitro studies plasma from dogs 2 and 3 obtained two days after ingestion of naphthalene was mixed with whole blood from a normal dog and incubated for one hour at 37 C. There was no change in the red blood count at the end of that time, but Heinz bodies were noted in the test specimen though they were absent in the saline control.

TABLE 2.—*Hematologic Data on Dogs*

	Days	Naphthalene Dosage (Gm.)	Hemoglobin	Red Blood Count (Millions)	Hematocrit	Reticulocyte Count (%)	White Blood Count	RBC Fragility	Heinz Bodies (%)	Remarks
Dog 1	0	0	13.1	6.78	41.5	0.2	14,400	.....	..	Venesection of approximately 60 cc. for blood studies; cystostomy
Weight	1	0.5	....	....	....	...	.....	.....	..	
15 lb.,	2	1.0	11.5	5.50	37.0	0.2	13,250	.....	0	
6.8 Kg.	3	2.0	11.5	5.43	37.0	0.1	13,700	.....	0	
	4	3.0	10.5	4.92	33.0	0.1	13,400	.....	0	
	5	2.0	10.7	5.25	35.0	0.1	25,500	.....	87	Diarrhea
	6	2.0	10.2	4.20	33.0	0.1	32,000	.....	96	
	7	2.0	5.6	2.75	20.5	0.1	32,400	.....	..	Listless
	8	0.0	3.4	2.00	13.0	3.8	28,000	.....	77	
	9	0.0	2.4	1.30	7.5	9.0	85,000	.....	70	Anorexia
	10	0.0	2.2	1.24	7.5	14.9	119,000	Control	49	
	12	0.0	3.5	1.73	15.0	33.8	38,000	0.54 to 0.39	13	Ataxic
	18	0.0	7.2	3.75	22.5	23.0	11,150	Dog 1	0	More active
	22	0.0	9.8	4.20	31.5	7.7	11,250	0.60 to 0.30	..	Asymptomatic
	36	0.0	11.6	4.70	....	0.2	9,300	.....	..	Ataxia subsiding
Dog 2	0	...	9.3	4.5	30.5	0.1	23,650	0.52 to 0.42	0	
Weight	1	3.0	....	....	....	...	.....	.....	..	
16 lb.,	2	...	9.1	4.40	31.0	0.1	49,200	.....	69	Listless
7.3 Kg.	3	...	8.1	3.94	27.0	0.1	29,700	0.61 to 0.45	68	
	4	...	7.1	3.34	23.5	0.3	47,000	.....	65	
	7	...	6.7	2.90	22.0	13.4	57,450	.....	39	
	8	...	6.6	2.79	24.0	14.7	.....	.....	33	
	10	...	8.3	3.60	27.5	10.1	36,400	.....	3	
	12	...	9.2	4.75	....	14.0	25,000	.....	0	
	14	...	9.6	5.22	34.0	9.0	.....	.....	..	
	17	...	10.5	?	36.3	5.6	31,100	.....	..	
	22	...	12.5	5.14	39.5	1.9	25,600	.....	..	
	25	...	12.9	5.30	40.0	1.1	17,500	.....	..	
	31	...	13.2	5.50	43.5	1.4	17,750	.....	..	
	36	...	14.9	5.74	46.0	0.7	19,000	.....	..	
Dog 3	0	...	14.4	6.63	49.0	0.1	15,400	0.49 to 0.40	0	
Weight	1	9.0	....	....	....	...	.....	.....	..	
13 lb.,	2	...	14.5	6.50	49.0	0.2	17,750	.....	94	
5.9 Kg.	3	...	14.5	6.40	47.8	0.1	16,300	0.61 to 0.42	91	Listless Vomiting Diarrhea
	4	...	13.7	5.92	45.0	0.4	15,950	.....	92	
	7	...	10.1	5.00	33.0	1.2	16,600	.....	79	
	8	...	10.2	4.65	34.0	2.2	20,500	.....	76	
	10	...	9.9	4.43	33.0	4.7	16,900	.....	42	
	12	...	10.0	4.57	....	9.0	13,650	.....	20	
	14	...	10.2	5.04	34.0	...	.....	.....	..	
	17	...	9.7	?	32.0	...	14,450	.....	5	
	22	...	11.1	4.26	34.0	4.2	16,250	.....	0	
	25	...	11.9	4.53	36.0	3.7	11,650	.....	..	
	31	...	13.7	5.33	43.8	2.5	14,200	.....	..	
	36	...	14.4	5.80	45.0	1.5	9,750	.....	..	
	51	...	15.0	5.75	47.5	0.1	15,500	.....	..	

COMMENT

To our knowledge the American literature contains no records of hemolytic anemia attributable to naphthalene poisoning. Most of the standard textbooks on pediatrics state that the substance is not soluble, passes through the digestive tract without absorption and is therefore harmless.[3] Textbooks on toxicology, however, refer to cases described in the foreign literature in which gastrointestinal and neurologic symptoms and anemia followed the ingestion of naphthalene.[4]

3. Mitchell-Nelson: Textbook of Pediatrics, ed. 4, Philadelphia, W. B. Saunders Company, 1948. Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1948.
4. McNally, W. D.: Toxicology, Chicago, Industrial Medicine, 1937.

Goetze in 1884 [5] observed restlessness, delirium, twitchings and cyanosis in a patient who had received large amounts of naphthalene, 6 to 7 Gm. daily for six days. On the seventh day the urine was black. Blood studies were not made.

Nash [6] briefly reported the development of urinary frequency, passage of black urine, diarrhea, transient anuria and headache and abdominal pain in a boy 13 years of age who had eaten a single moth ball. Unfortunately no data on the blood were given.

Prochownik [7] reported a fatal case of naphthalene poisoning in a boy 6 years of age who had received seven doses of 0.25 Gm. naphthalene as treatment for oxyuriasis. Within two days the child became restless and disoriented and began to vomit. The spleen became enlarged and icterus developed; the urine was scanty and contained hemoglobin and albumin. The patient died the following day.

Heine [8] described a woman who had taken seven consecutive doses of 0.4 Gm. of naphthalene for the treatment of oxyuriasis. Dysuria, weakness, drowsiness and numbness of the extremities developed within two days. The patient passed black urine, and her skin

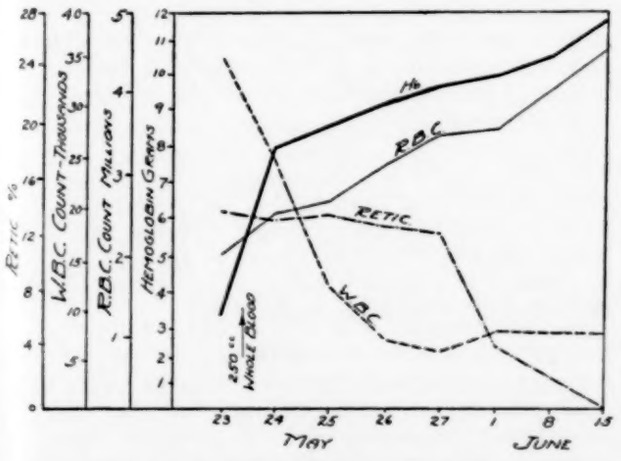

Fig. 2 (case 4).—Essential hematologic data during the period of observation.

became icteric. Liver and spleen were palpable. The urine contained hemoglobin and albumin. The patient recovered.

Anemia of hemolytic type similar to that observed in our patients was reported by Smillie [9] in Brazil in 4 patients who had received beta-naphthol. Because a group of 77 other patients who had been given the same drug in comparable doses failed to exhibit anemia, Smillie concluded that special predisposing factors were required for the development of toxic effects.

Taylor and Russel [10] recorded anemia, icterus and hemoglobinuria in an African Negro who had ingested two moth balls five days earlier.

Konar, Roy and De [11] described the case of a man aged 24 who had taken an unknown amount of naphthalene, mistaking it for candy. Two days later the patient became pale, icteric and semicomatose. The hemoglobin on the fourth day was 30 per cent, the red blood count 2,410,000 and the white blood count 31,200. The urine was brown but gave a negative test for occult blood. The patient died, and naphthalene was demonstrated in the tissues, stomach contents and urine. The liver showed patchy necrosis.

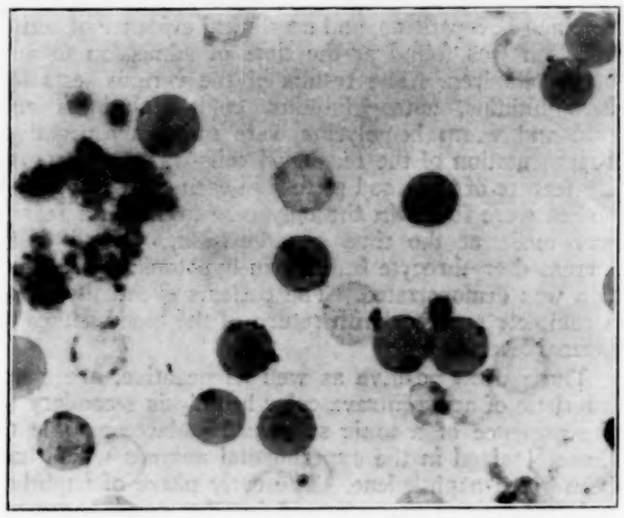

Fig. 3 (dog 1).—Blood smear on fifth day after the first dose of naphthalene showing Heinz bodies in erythrocytes (cresyl blue stain).

The results of our animal experiments leave little doubt that naphthalene is a toxic substance capable of being absorbed and of producing an anemia of hemolytic type. The order of events—the appearance of Heinz bodies preceding a sharp fall in hemoglobin, hematocrit and red blood count; fragmentation of erythrocytes; leukocytosis and reticulocytosis, and subsequent restoration of the blood values to normal levels—is characteristic for the effect of a hemolytic poison comparable to the well known action of phenylhydrazine.

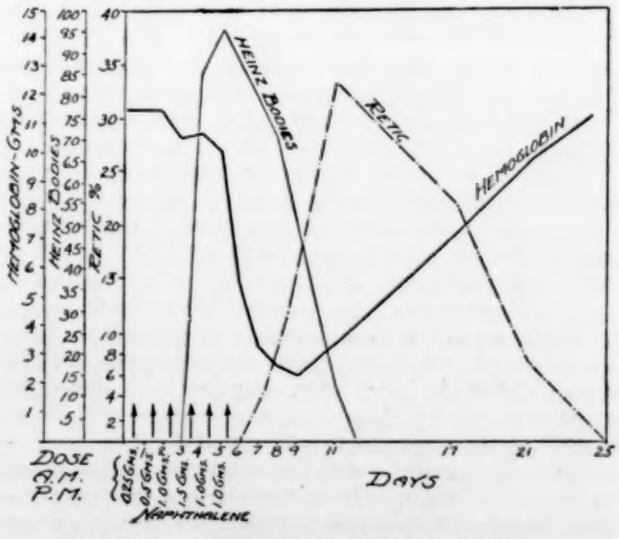

Fig. 4 (dog 1).—Hematologic response to naphthalene.

In each of the 4 patients described by us a definite history of naphthalene ingestion was obtained, although the exact amounts could not be established. In 1 case absorption was demonstrated by isolating naphthalene derivatives in the urine. Each child had previously been in perfect health and had not been exposed to

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other chemicals with hemolytic action. Within a period varying from three to seven days, severe hemolytic anemia developed in each case, and in 3 of the 4 patients hemoglobinuria was observed. In the fourth case a history of passing dark "orange" urine suggested that hemoglobinuria may have been present before admission. The plasma oxyhemoglobin was elevated in all 4 patients. No history of infection was obtained in 3 patients, and no clinical evidence of active infection was found at the time of admission in any of the children. The results of the various tests for isoagglutinins, autoagglutinins, cold agglutinins and cold and warm hemolysins were uniformly negative. Fragmentation of the red blood cells was an outstanding feature of the blood picture in each case, and Heinz bodies were found in the only case in which a search was made at the time of admission. In all cases increased erythrocyte fragility in hypotonic saline solution was demonstrated. The patients eventually made a complete recovery with return of the blood values to normal levels.

These data, positive as well as negative, are characteristic of acute intravascular hemolysis secondary to the presence of a toxic substance and comparable to those obtained in the experimental animals which had been given naphthalene. The early phase of naphthalene poisoning, characterized by the development of Heinz bodies in the experimental animals, was, of course, not studied in the human subjects, who were hospitalized only after the severe anemia had already developed.

The mechanism of hemolysis induced by naphthalene is not entirely clear. It is evident that the substance is absorbed in the gastrointestinal tract. The quantitative aspects of absorption are unknown and may be highly variable. According to Stekol,[12] naphthalene is partly excreted into bile by the liver and partly detoxified by oxidation to beta-naphthol and conjugation with glycuronic, sulfuric and mercapturic acids. The conjugates are excreted by the kidneys. Such naphthalene as has escaped detoxification enters the general circulation. From our limited experiment, which consisted in exposure of normal erythrocytes to the patient's serum and production of Heinz bodies in canine erythrocytes exposed to serum from a poisoned animal, it would appear that naphthalene in the form of soluble compounds causes hemolysis in vitro by direct action on red cell membranes.

Several observers have commented on the differences in dosage of naphthalene tolerated by different persons. Variations in the absorption and the efficiency of detoxification by the liver may explain these discrepancies.

The general picture strikingly resembles that of so-called Lederer's anemia or acute hemolytic anemia of unknown origin. It is therefore noteworthy that the history of moth ball ingestion in our cases was obtained only after specific questioning and was not brought out by routine questions regarding chemicals, poison or drugs. Had the information concerning naphthalene not been obtained, each case undoubtedly would have been labeled Lederer's anemia. It is likely that some cases reported in the literature under that title were in reality instances of naphthalene poisoning. Lederer's anemia is often attributed to infection, chiefly because of the concomitant symptoms of fever, lethargy, leukocytosis and gastrointestinal manifestations. It is obvious that these phenomena can be produced by the severe hemolytic process itself.

The diagnosis of naphthalene poisoning depends primarily on an accurate history. It will be aided by a consideration of the age incidence. All our patients were approximately 2 years old, an age group particularly prone to the ingestion of household poisons. The clinical symptoms begin with listlessness and anorexia followed by vomiting and other gastrointestinal disturbances . Eventually pallor is noted and hemoglobinuria occurs, if the condition is severe.

Among physical observations the absence or slight degree of splenomegaly and the absence of appreciable icterus appear significant.

The laboratory results are those of severe acute hemolytic anemia and usually hemoglobinuria. The brown color of the plasma, probably denoting the presence of methemalbumin, should suggest sudden intravascular hemolysis. Free hemoglobin is demonstrable in the plasma in the acute phase. Fragmentation of red blood cells and the presence of Heinz bodies are characteristic features of toxic hemolysis. Urinalysis shows hemoglobin, albumin and occasional leukocytes and granular casts. An odor of naphthalene in urine and stools should be looked for in suspected cases.

The management of the condition obviously does not include splenectomy, and an accurate etiologic diagnosis is therefore of prime importance. The treatment of choice consists of transfusions as indicated by the blood studies. In the presence of hemoglobinuria it would seem wise to give alkalis in amounts sufficient to produce an alkaline urine, even though the effectiveness of this measure is doubtful.

SUMMARY

Attention is called to the occurrence of severe hemolytic anemia and hemoglobinuria as the result of naphthalene ingestion, and 4 pertinent cases are reported. Hemolytic anemia preceded by the appearance of Heinz bodies in the erythrocytes was produced in dogs. Heinz bodies were also produced in vitro by exposing normal canine erythrocytes to the plasma of dogs who had been fed naphthalene. A review of the literature disclosed a small number of cases of anemia and hemoglobinuria following naphthalene intoxication reported exclusively in the foreign literature. The condition arises chiefly in children as the result of accidental poisoning, and in view of the availability of moth balls, it may be commoner than heretofore believed. Differentiation from so-called Lederer's anemia is difficult unless a history of ingestion of naphthalene is specifically elicited.

5224 St. Antoine Street.

12. Stekol, J. A.: The Metabolism of Naphthalene in Adult and Growing Dogs, J. Biol. Chem. **110:** 463, 1935. Stekol, J. A., and Mann, F. C.: Studies on the Mercapturic Acid Synthesis in Animals, ibid. **117:** 619, 1937.

Vitamin B Complex Deficiency.—Early signs of endemic vitamin B complex deficiency, and also of experimentally induced deficiency, include non-specific complaints such as decreased appetite, easy fatigability, lack of ambition and nervousness as well as personality disturbances, including irritability, moodiness, depression, vague fears, lassitude and quarrelsomeness. In acute experimental deficiency, outstanding manifestations are disinclination to spontaneous activity, and personality alterations of psychoneurotic type, i. e., depression hypochondriasis and hysteria. Long before these symptoms appear, the urinary excretion of the B vitamins has fallen to low levels.—Grace A. Goldsmith, Chemical Measurements in Relation to Physical Evidence of Malnutrition, *Federation Proceedings*, June, 1949.

TOPICAL BACITRACIN THERAPY OF PYOGENIC DERMATOSES

A Clinical Report

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and
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The literature is replete with evidence of the high index of allergenicity of the more effective agents used in the therapy of the various pyodermas. The alarming incidence of the apparent induction of hypersensitivity to such valuable medicaments as sulfonamide drugs and penicillin when they are used topically to treat the minor dermatoses, thus vitiating their future usefulness in generalized and systemic infections, has prompted the cautioning editorial by Sulzberger and Baer in the "Year Book of Dermatology." [1] It is therefore expedient that information concerning the useful and less allergenic therapeutic agents be promulgated widely. We are reporting some significant clinical results which we have noted following the topical administration of a new antibiotic, bacitracin. These results corroborate the findings of Miller, Slatkin and Johnson reported recently in the *Journal of Investigative Dermatology*.[2]

HISTORICAL DATA

In *Science* (Oct. 12, 1945) Johnson, Anker and Meleney [3] reported the recovery of a new antibiotic, bacitracin, from a strain (Tracy I) of Bacillus subtilis. It was active in vitro mostly against gram-positive organisms and the Gonococcus and Meningococcus. In vivo studies showed that it protected mice against experimentally induced hemolytic streptococcic infections and guinea pigs against experimentally induced gas gangrene infections. Meleney and Johnson [4] reported 100 surgical infections treated locally by topical applications and direct injection of bacitracin into furuncles, carbuncles and deep and superficial abscesses. An ointment containing the antibiotic was used for open lesions. The results were favorable in 88 per cent of the cases, and response was rapid. Bacitracin did not cause irritation of the conjunctiva. It was not locally toxic or irritating and its activity was not inhibited by plasma, blood, pus, broken down tissue or organisms which produce penicillinase. They concluded that bacitracin would be of value if it succeeded where penicillin and sulfonamide compounds did not.

Scudi and Antopol [5] studied the toxicity of bacitracin in mice and rats. Intraperitoneal toxicity was greater in rats than in mice. They found that the subcutaneous LD_{50} was two to seven times the intraperitoneal LD_{50}. A dosage of 3.75 Gm. per kilogram failed to produce death. Mice receiving one, ten and twenty-five times the therapeutic dose for five days gained in body weight. Tests with isolated guinea pig ileum indicated that bacitracin contains a minute amount of histamine-like substance.

From studies on the absorption and excretion of bacitracin in the dog, Scudi, Clift and Krueger [6] determined that bacitracin is destroyed in the gastrointestinal tract. Following its subcutaneous, intramuscular and intravenous injection high levels of the agent were obtained in the blood. The concentration fell least rapidly after subcutaneous injection. No toxic symptoms were observed following subcutaneous or intramuscular injections. Rapid intravenous injection of large doses produced nausea and muscular spasm. Small doses produced no such effect. Urinary excretion following parenteral administration of bacitracin appeared to increase with the dose but varied widely, from 7 to 98 per cent of the dose administered. High concentration in the urine persisted for more than seven hours. Bacitracin did not penetrate the red blood cells. Low spinal fluid concentrations as compared with serum concentrations were obtained in studies made with 5 monkeys.

Results of Bacitracin Therapy in One Hundred and Thirty-Eight Cases of Pyogenic Disease

Disease	No. of Cases	Cured	Improved	Failed	Minimum and Maximum No. of Days Required for Cure	Average No. of Days Required for Cure
Impetigo	46	46	—	0	2 to 10	4.7
Ecthyma	55	55	—	0	2 to 35	11
Infectious eczematoid dermatitis	15	15	—	0	3 to 39	9
Folliculitis	11	7	3	1	4 to 28	15
Sycosis vulgaris	4	1	1	2	—	21
Hidradenitis suppurativa	2	0	0	2	—	—
Decubitus ulcers	3	3	—	0	14 to 32	25
Pyoderma gangrenosum	1	1	—	0	—	67
Bismuth slough	1	—	1	—	Marked improvement of indolent lesion within 2 wks.	

Eagle and associates [7] determined that the total urinary excretion of bacitracin in man was 87 per cent in six hours; the rate of excretion in the first hour was one-third that of penicillin G, but after two hours excretion of bacitracin was more than five times as rapid. The serum concentration of the agent following intravenous or intramuscular injection varied in linear proportion to the dosage. In man, levels two hours after injection were four times greater than the average observed with penicillin G. Therapeutic levels of bacitracin were maintained for 2.5 to 6.8 hours as compared to 1.2 and 2.1 hours with penicillin.

More recent investigation of the effect of bacitracin has contraindicated its parenteral administration in man because of its high renal toxicity. Presently, the oral administration of bacitracin in amebic dysentery indicates that it may well be a new and valuable amebacide. Confirmatory investigation is now in progress.

Bacitracin used in this study was donated by Commercial Solvents Corporation, New York.

Instructor in Dermatology, Georgetown University School of Medicine, and attending staff physician, Walter Reed General Hospital (Dr. Derzavis).

The opinions expressed are those of the authors and are not to be considered the official opinion of the medical department of the United States Army.

Clinical studies herein reported were carried out at the Walter Reed General Hospital and in the Division of Dermatology, Georgetown University Service, Gallinger Municipal Hospital.

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3. Johnson, B. A.; Anker, H., and Meleney, F. L.: Bacitracin; A New Antibiotic Produced by a Member of the B. Subtilis Group, Science **102**: 376 (Oct. 12) 1945.
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ALLERGENICITY

To determine the human sensitivity to bacitracin, 150 adults were patch tested with bacitracin ointment (1,000 units per gram of petrolatum) for forty-eight hours. All tested areas were negative for reaction. A fortnight later, 50 of these previously tested persons were retested by the patch method on the same or approximate sites for another forty-eight hour period. All test sites were again normal after the patches were removed.

These results seemed indicative of low allergenicity and were subsequently corroborated by the occurrence of only 1 case of dermatitis of the contact type among the 138 patients subsequently treated with bacitracin ointment. This unique patient was not only allergic to the ingredients of bacitracin ointment (bacitracin and petrolatum) but also reacted violently to liquid petrolatum, soybean oil bases, olive oil, wool fat, lard, greaseless ointment bases, carbowax,® quinoline, iodochlorohydroxyquinoline (vioform®) and sulfonamide compounds. He was able to tolerate penicillin solution topically and penicillin parenterally in a vehicle of oil and wax.

MATERIAL AND RESULTS

Since we were interested in a comparison of the topical therapeutic and sensitizing potencies of bacitracin, penicillin and the sulfonamide drugs on dermatoses, only diseases (namely, the pyodermas) which respond well to the last two medicaments were considered. A total of 138 patients were treated, and data given are in the accompanying table.

COMMENT

It is our impression that bacitracin is the most effective agent we have used in the therapy of superficial streptodermas and staphylodermas. Response to this topically applied agent is at least as rapid as responses to sulfonamide compounds, penicillin, chlorohydroxyquinoline, iodochlorohydroxyquinoline nitrofurazone (furacin®) and ammoniated mercury. More important is the extremely low incidence of allergenicity of the bacitracin preparation used in this investigation. The only instance of dermatitis venenata occurred in a patient with pyoderma and chronic lymphatic leukemia who was hypersensitive to a multiplicity of therapeutic agents.

The direct contact of bacitracin with the infected area is evidently necessary to effect a cure. This is evident in the rapid response of such superficial pyodermas as impetigo contagiosa and infectious eczematoid dermatitis. Contrariwise, the deeper folliculitides, including sycosis vulgaris and hidradenitis suppurativa, exhibited failures in roughly the same proportion as we had experienced with other antibacterial agents. Of particular note is the exceedingly rapid response in most cases of impetigo contagiosa. Many of these eruptions were dry and cured within forty-eight hours of the initiation of therapy.

Attention is directed toward the healing effect of bacitracin ointment on decubitus ulcerations in 3 instances. These patients (an amputee, a paraplegic and a cancer victim) had received numerous therapeutic routines and agents with poor responses. Bacitracin ointment has retained a prolonged healing effect in all 3. In 1 case of pyoderma gangrenosum there was rapid improvement in the existing lesions, but complete healing without new lesions did not occur until the associated ulcerative colitis was effectively controlled.

It is interesting to contrast the rapid effectiveness of bacitracin incorporated in petrolatum with that of other antibacterial agents administered in a simple grease base. Ammoniated mercury, for example, may be ineffective in petrolatum; whereas, although the miscibility of our greasy ointment with the watery exudate of impetigo contagiosa was poor, the curative effect was rapid. The therapeutic potency of bacitracin must indeed be extremely high.

SUMMARY AND CONCLUSION

One hundred and thirty-eight patients with deep and superficial pyodermas were treated with an ointment consisting of 1,000 units of bacitracin per gram of petrolatum. Response to therapy was rapid and effective in all lesions wherein direct contact with the bacitracin ointment was obtained.

There was only 1 proved case of hypersensitivity to this new antibiotic among the 288 patients (138 clinical and 150 patch test cases) in this study.

It may be concluded that bacitracin is a new and potent agent for the treatment of the accessible pyodermas. Of particular note is its extremely low index of allergenicity as evident in results obtained at this time.

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Clinical Notes, Suggestions and New Instruments

POISONING DUE TO TETRAETHYLPYROPHOSPHATE

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When allied teams entered Germany after the war, they found the Germans using, for control of aphids, an insecticide which had been developed as a substitute for nicotine. The active ingredient of this compound was tetraethylpyrophosphate (TEPP), a powerful cholinesterase inhibitor. This insecticide recently has been made available in this country, one of the commercial preparations being vapotone-XX.® The label of the manufacturer [1] lists the ingredients as tetraethylpyrophosphate 20 per cent, related organic phosphates 30 per cent and inert ingredients 50 per cent. Recently a case of poisoning due to agricultural use of this compound was encountered.

REPORT OF CASE

A Negro aged 17 was admitted on the evening of June 14, 1949, retching, salivating profusely and in a semistupor. It was difficult to obtain an adequate history, and all that could be learned was that he had been spraying melons with vapotone.® The next day a more complete history was obtained. Shortly after eating his noon meal, he had begun to spray with this compound, diluted 7 ounces to a gallon of water (0.21 liter to 3.78 liters). He had used it before without ill effects, although this time the can leaked more than usual and his back became wet. About 2:45 p. m. he sliced a melon and ate it without washing his hands. The slices were cut lengthwise, and his hands would have touched the portions that he later ate. When he was finished eating he sliced a piece for his companion, but this other boy did not subsequently become ill. About fifteen minutes later he became weak

1. A communication received from the manufacturer after preparation of this paper gives the composition of the insecticide in detail. Xylene is used as a diluent, apparently accounting for the odor noted on the patient's breath. The "related phosphates" are other ethyl phosphates, but a more exact composition is not stated. A copy of the label sent with their letter contains much more detailed information than was available on the material used by the patient. It recommends use of protective clothing, rubber gloves and respirators and discusses toxic symptoms. The recommended dilution is ½ pint to 100 gallons (0.24 liter to 378 liters). As can be seen, this patient used an extremely strong solution and took not even elementary precautions.

and was unable to see; there was a tightness in his chest, abdominal cramping, diarrhea and vomiting. On admission the blood pressure was 150 systolic and 90 diastolic, the pulse rate 56, strong and bounding, and the respiratory rate 24. His breath had a characteristic and familiar, although never definitely identified, odor, which may have been due to the solvent. His pupils were extremely constricted, being less than 1 mm. in greatest diameter. There was profuse salivation, about 2 ounces (60 cc.) of saliva being produced within a thirty minute period. Although he answered questions adequately, there was an apparent drowsiness and disinterest. He vomited occasionally, but there was no abdominal rigidity. The deep reflexes were generally hypoactive, and no pathologic reflexes were present; however, after a tendon had been struck there were slow, repeated tendon jerks, six to eight in number, about one-fourth to one-half second apart. All over the body there was a slow wavelike contraction of the muscle bundles. There was twitching of the fingers and corners of the mouth. The spinal fluid pressure was 160 mm. with no cells, the protein level was 43 mg., sugar 76 mg. and chlorides 672 mg., per hundred cubic centimeters. The white blood cell count was 13,000, with 90 per cent polymorphonuclear cells. The hematocrit reading was 43. Urine had a specific gravity of 1.018 with no sugar or albumin and a normal microscopic appearance. The blood sugar determination was 143 mg. per hundred cubic centimeters, the carbon dioxide-combining power 48 volumes per cent, the chlorides 516 mg. and the blood urea nitrogen 15 mg. per hundred cubic centimeters. The next morning there was still some abdominal cramping and vomiting, but by afternoon all symptoms had disappeared. The blood urea nitrogen on June 20 was 29 mg. per hundred cubic centimeters, but two days later it had dropped to 11 mg. Liver function tests showed negative cephalin flocculation and a normal thymol. There were no mental symptoms except for the aforementioned drowsiness at any time. He was discharged on June 22 with no residual symptoms.

COMMENT

Tetraethylpyrophosphate is an irreversible inhibitor of cholinesterase, the effects lasting for twenty-four to thirty-six hours. Except for a shorter duration of action, its pharmaceutic effect is essentially the same as that of diisopropylfluorophosphate, which has been used for some time in physiologic research. As can be seen, the foregoing symptoms are typical of the postulated effect of an excess of acetylcholine at cholinergic nerve endings—a stimulation of the constrictor pupillae, of salivary glands, of the sphincter at the cardiac end of the esophagus, of smooth muscle in blood vessel and intestinal walls, and of skeletal muscles generally. Burgen and associates [2] have stated that in toxicity experiments 1 to 3 mg. of tetraethylpyrophosphate per kilogram of body weight produces hyperexcitability, twitching, salivation and convulsions. The lethal dose for rats is 2 mg. per kilogram orally and 40 mg. per kilogram on the skin. Hexaethyltetraphosphate is a related compound, the effect of which may depend on hydrolysis to tetraethylpyrophosphate. The former is one-half to two-fifths as toxic as the latter. If it is assumed that the related phosphates mentioned on the insecticide label have about the same range of toxicity as hexaethyltetraphosphate and that 1 mg. of tetraethylpyrophosphate per kilogram of body weight is sufficient to produce the symptoms noted, the oral dose of the dilution which the patient used would need to be 3.6 cc., or the amount on the skin approximately 70 cc., or any comparable combination of the two. The commercial preparation is labeled poison, but the label does not mention the possibility of absorption of the product through the skin or antidotes effective against the compound.

Because the composition of the preparation could not be learned at the time of admission, and because the patient stated that he was attempting to kill plant lice (for which nicotine is often used) and had symptoms similar to those of nicotine poisoning, it was assumed that his symptoms were due to nicotine and no treatment was given. A telegram from the Food and Drug Administration the next day stated that the antidote for tetraethylpyrophosphate is atropine, 1/100 grain (0.6 mg.), to be repeated until dilatation of the pupils takes place, plus anticonvulsive treatment.

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SUMMARY

A case of poisoning with a potent new insecticide in the group of the cholinesterase inhibitors is reported. In view of the small dose necessary to produce symptoms and the possibility that poisoning may occur through cutaneous absorption of the compound, it is recommended that practitioners be on the lookout for such cases and that commercial compounds of this type be labeled to impart more detailed information for the protection of their users.

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UNUSUAL REACTION TO ANT BITES

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On July 12, 1949, Staff Sergeant W. J. M. reported to the dispensary, Station Hospital, Randolph Field, Texas, in extreme distress; he was able to blurt out that he had been bitten by ants. His entire body was covered with an urticarial rash; his eyes were swollen nearly shut; he was clawing frantically at his chest, arms and neck, and his breathing was stertorous and accompanied by a frothy, mucous expectoration from the mouth. He was cyanotic and appeared to be on the verge of shock.

The patient was given 0.4 mg. of epinephrine; he was stripped and showered to remove ants which were on the upper part of the arm, and he was then given oxygen. The chest was full of moist rales, and preparations were made to perform a tracheotomy. However, his breathing became less labored and he was given 100 mg. tripelennamine hydrochloride (pyribenzamine hydrochloride®) orally. Relief was of short duration, and it was decided to give the patient intravenous procaine therapy, which was started at once. Three hundred milligrams of procaine hydrochloride in 300 cc. of 5 per cent dextrose was given slowly, with almost instant relief from symptoms. However, paroxysms (four in all) recurred during treatment, but at the end of two hours the patient was quiet and the rash had disappeared. The patient slept until evening, when he ate an average meal. His only complaint was of slight substernal soreness. The next day the patient gave the following history:

On the day of the attack, the patient finished preflighting a plane and sat down, resting his bare arm on the runway curbing. He felt the ant bites and almost immediately began to itch and felt his eyes start to swell. He started for the hospital but did not make it and was picked up in a car and brought in. His first attack of this nature had occurred in 1945, when he was bitten by an unknown insect while he was in military service on Guam. He was hospitalized for a week with identical symptoms; he stated that he had received injections of epinephrine almost hourly for relief. In 1948 he lost three fingers in a hunting accident and was given gas gangrene antitoxin in a civilian hospital. This, too, was followed by a similar episode, although the respiratory embarrassment was much less and the duration was only five days. He further stated that mosquito bites cause a severe local reaction, but that as a child he was stung by bees and wasps without any particular disability.

From an etiologic point of view, it is possible to postulate that insects which cause this patient distress either inject a protein with the bite or break down homologous protein to produce the reaction. Whatever the mechanism, the patient released histamine when bitten by ants and this reaction was controlled with epinephrine, tripelennamine and procaine. The amount of epinephrine used and the temporary nature of the relief afforded by this drug would rule this out as the therapeutic agent of choice. It is difficult to determine which of the other two compounds was specific. Possibly either alone might have produced the cure. Unfortunately, the distress of the patient was too great to permit a good clinical test of tripelennamine alone, which apparently gave some relief from symptoms.

From the medical service, Station Hospital, Randolph Air Force Base, Randolph Field, Texas.

POSITIVE METHYL ALCOHOL REACTIONS IN THE TISSUES OF A YOUNG PERSON DYING IN DIABETIC COMA

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This report describes the presence of a substance giving the color reactions of methyl alcohol in the tissues of a young girl dying of diabetes mellitus complicated by acidosis and coma. As far as the authors are aware, such a finding has not previously been reported.

The circumstances surrounding the death did not permit an orderly elicitation of the facts. This explains the gaps in the evidence needed to fulfil all the criteria for an absolute diagnosis of diabetes mellitus. The facts, however, are adequate to support such a diagnosis.

REPORT OF CASE

A white girl aged 15 was admitted to a hospital at 1:30 a. m. in stupor. The father stated that for the past few weeks the girl had been losing weight, although she had been eating fairly well. About one week before admission to the hospital she had consulted a physician because her menses had not begun. She was given an injection of an endocrine substance. Three days before admission she began to complain of mild abdominal pains tending to be localized in the right upper quadrant. Despite this, she went to a children's party that same evening and consumed a large amount of ice cream, candy, cake and soda. The next day she revisited the physician because of the abdominal pains and slight vomiting. She was given a second subcutaneous injection of an endocrine preparation, and a dextrose solution was administered rectally to control the vomiting. The endocrine preparation and the dextrose solution were later analyzed but did not give methyl-alcohol-like reactions. The mild abdominal pains persisted for another two days. When the girl went into stupor the family brought her to the hospital.

On admission it was noted that she was an underdeveloped and undernourished young girl whose tongue was remarkably dry. The rectal temperature was 98.6 F., the pulse rate was 120 per minute and the respiratory rate was 25 per minute. The abdomen was slightly rigid, but there was no distention, tenderness or rebound tenderness. The remainder of the physical examination revealed normal conditions. The white blood cell count was 16,400 with 80 per cent polymorphonuclear leukocytes and 20 per cent lymphocytes. The hemoglobin content was 93 per cent. An infusion of 1,000 cc. of 5 per cent dextrose in isotonic sodium chloride solution was started, being completed several hours later. The temperature remained normal, but the pulse and respiratory rates increased, the former averaging 140, the latter 35 per minute. Eight hours after admission the patient had a severe convulsion which lasted several minutes and was followed by several slight convulsions. She died nine hours after admission. Urinalysis made several hours after the infusion had been started revealed a sugar content of 1 per cent and gave a 2 plus reaction for acetone.

Autopsy revealed a somewhat underdeveloped young girl who was notably undernourished. The only gross observations of note were an occasional petechial hemorrhage in the leptomeninges and general visceral congestion. Pieces of each tissue were fixed in 4 per cent formaldehyde solution, embedded in paraffin and stained with hematoxylin and eosin.

Histologic examination of the pancreatic tissue disclosed that in an occasional island of Langerhans some of the cells contained large eosinophilic hyaline droplets. The liver was normal except that many of the periportal liver cord nuclei revealed the vacuolar changes associated with glycogen deposition. The number of nuclei manifesting this change was distinctly more than that occasionally observed in the liver of a nondiabetic person. In the kidney the cytoplasm of the epithelial cells of the loops of Henle exhibited advanced vacuolar changes. The brain revealed an occasional petechial hemorrhage in the leptomeninges.

From the office of the Chief Medical Examiner, City of New York.

A routine analysis of the stomach contents and brain for all poisons and of the liver and kidneys for metallic poisons resulted negatively, except in the brain there were small amounts of a substance which gave the reactions of methyl alcohol.[1] Faint traces of this substance were also found in the stomach contents. Five hundred grams of brain and one half of the stomach contents (about 1 ounce, 28 Gm.) were steam-distilled separately. In each instance 100 cc. of steam distillate were collected. The distillate was oxidized with a red hot copper spiral. This procedure oxidizes methyl alcohol to formaldehyde. The following tests were made on the oxidized and unoxidized distillates.

1. Distillate plus phenylhydrazine hydrochloride plus sodium nitroferrocyanide plus sodium hydroxide. A blue color which gradually faded denoted the presence of formaldehyde.

2. Denigès' test. To the distillate was added concentrated sulfuric acid and then Schiff's reagent. The presence of formaldehyde was indicated by a violet red color.

3. Hehner's test. To the distillate was added an equal volume of milk and a trace of ferric chloride. The mixture was strongly acidified with hydrochloric acid and then heated in a boiling water bath. A violet color denoted the presence of formaldehyde.

With each test the unoxidized distillate gave a negative reaction and the oxidized distillate a positive reaction for formaldehyde. A special investigation by one of us as well as by the police revealed no possible source where the girl might have obtained methyl alcohol. There was no familial history of diabetes.

COMMENT

The diagnosis of diabetes mellitus is well substantiated by the histologic observations and the clinical history. The combination of eosinophilic droplets in the cells of the islands of Langerhans, vacuolar swelling of the periportal liver cord cell nuclei and vacuolar cytoplasmic changes in the loops of Henle is found only in untreated diabetes mellitus.

The tests applied to the oxidized distillate gave the color reactions of formaldehyde. In tests of the unoxidized distillate results were all negative. Methyl alcohol is claimed to be the only substance known at the present time which is volatile with steam and which when oxidized with a red hot copper spiral will give all these results.[2] This indicates that methyl alcohol or a substance giving the same reactions had been distilled out of the tissues. Whether the substance was originally present in the tissues in the free state or whether it is a hydrolytic, degradation or other type of product must still be determined.

This observation is important in forensic medicine. It emphasizes the necessity of ruling out diabetic acidosis in all cases in which the color tests indicate the presence of small amounts of methyl alcohol and certainly in all sporadic cases, particularly when the source of methyl alcohol has not been determined. Death can probably be attributed to the exogenous poison when the presence of large quantities of methyl alcohol is revealed by the color reactions.

There is little point in speculating at this stage where the substance giving positive colorimetric reactions for methyl alcohol fits into the intermediary metabolism of foodstuffs in the patient with diabetes mellitus complicated by acidosis and coma. Whether similar tests can be obtained in the tissues of those dying from diseases complicated by acidosis must still be determined.

SUMMARY

1. Positive colorimetric reactions usually produced by methyl alcohol were obtained in the steam distillate from the brain of a young girl whose death resulted from diabetes mellitus complicated by acidosis and coma.

2. The importance of this observation in medicolegal investigations is discussed.

1. Gonzales, T. A.; Vance, M., and Helpern, M.: Legal Medicine and Toxicology, New York, D. Appleton-Century Company, Inc., 1940.
2. Gettler, A. O.: Critical Study of Methods for the Detection of Methyl Alcohol, J. Biol. Chem. 42: 311, 1920. Autenrieth, W.: Laboratory Manual for the Detection of Poisons and Powerful Drugs, translated by W. H. Warren, Philadelphia, P. Blakiston's Son & Co., 1928.

Council on Pharmacy and Chemistry

REPORT TO THE COUNCIL

The Council has authorized publication of the following report from the Therapeutic Trials Committee, a standing Committee of the Council on Pharmacy and Chemistry.

AUSTIN SMITH, M.D., *Secretary.*

PROGRESS WITHOUT STATISTICS

H. M. C. LUYKX, D.Sc.
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Among the functions of the Therapeutic Trials Committee is the encouragement of critical controlled clinical trials of new agents in the diagnosis, prevention and treatment of disease. Such trials must be pursued by recognized scientific methods, many of which involve the application of simple statistical procedures. Furthermore, data derived from such clinical trials frequently can best be assembled and presented with the aid of statistical technics. Hence, clinical investigators and readers of scientific journals should be familiar with the uses and limitations of the commonly used statistical methods and the interpretation which may safely be drawn from the results of the statistical treatment of data.

The Committee requested Dr. H. M. C. Luykx of New York University to prepare a general article on this subject. The Committee believes that the methodology of statistics is best left to the statistician but that the need for and interpretation of statistical procedures should be generally appreciated by the medical and allied professions. It is hoped that the following discussion, prepared by Dr. Luykx, will encourage investigators to seek the aid of statisticians in the design of experiments and the analysis of data and will enable those who read scientific periodicals to be more critical in their acceptance of the conclusions of the authors of articles.

WALTON VAN WINKLE JR., M.D., *Secretary.*

There was a time when medicine could not be dignified by the name of science. As factual knowledge has replaced unproved hypotheses, research has extended into the development of theory based on more and more exact—and more exacting—observations. Repeated observations have produced evidence not obtainable with a single measurement. From this has grown the use of numerical data as a powerful tool in demonstrating relationships not otherwise evident.

Numerical data have played such a large part in modern research that it is no great surprise to find them abused and endowed with an exaggerated importance, sometimes out of all proportion with their true worth. It is human nature to imbue the printed word with a sanctity far beyond that of a personal observation. In the same way, a numerical statement is often credited with a value not given to a verbal phrase, even though there may be no justification for such distinction. In the ordinary mind a numerical observation implies objectivity; it implies accuracy; it implies scientific value. If such implication is not intended, care should be taken to make this clear. If the implication is to be justified, the observer or analyst must be equipped to observe phenomena objectively and accurately, to present his observations clearly and to interpret his findings correctly.

OBSERVATION

Although the present remarks will refer chiefly to quantitative observations of various kinds, it is not to be assumed that they will concern the research worker only, and not the clinician. Clinical observations may be purely qualitative in nature, but their full value is seldom realized when taken singly. It is in comparison with, or in combination with, other similar observations that the solution of a particular problem may lie. For example, to observe the presence or absence of a rash may be of clinical significance. But, as the clinician well knows, the frequency with which a similar type of rash occurs, in the same or in other circumstances, forms the basis of knowledge concerning a given disease which a single observation does not provide. The important factor then is the definition by which similarity is established: the color of the rash, its anatomic distribution and its duration. Similarity and dissimilarity are the essence of classification, and the value of any classification or categorization is determined strictly by the adequacy and accuracy of the original observations.

It can be noted from the present literature that an ever increasing proportion of the studies on medical problems depends on quantitative data. When preliminary exploration has been completed, in any study of this kind the first step—which traditionally receives inadequate attention—is to plan, on the basis of (1) the specific questions to be answered, (2) the type and source of information available, (3) the manner in which observations can be made and recorded and (4) the type of presentation best suited to the problem—tables, graphs, averages, percentages and the like.

The matter of deciding on the specific questions to be answered may well be emphasized. There have been many instances in which an accumulation of data turned out to be relatively useless, because it had a bearing on a general subject but was not designed to answer a question which was formulated after the study was well under way. An example of this is a study in which 43 patients with rheumatoid arthritis received a given form of therapy, and the course of the disease was carefully observed in each instance. The treatment being by no means 100 per cent effective, it was logical to compare results with those reported from other studies. A proper comparison, however, was not possible, because this was not contemplated at the time the study was set up and no attempt was made to have comparable groups receiving different forms of therapy.

Although the questions to be answered will indicate the type of observations which ought to be made, it is the source of the data which will determine the observations which can be made. A laboratory problem may provide records consisting mainly of readings on various instruments, titration values, counts of animals and numbers of cells. In a survey of patients or cases, the observations are described by physicians, by patients themselves and so on. The objectivity of such observations varies over a wide range, and their adequacy must again be related to the questions to be answered. It should not be necessary to point out that such matters should be considered before a project is initiated. There is a wide discrepancy between what should be and what is.

Surveys and Samples.—In making a survey, the object is usually to accumulate information from which some sort of generalization can be made. The generalization will apply to a population larger than that from which the factual data have been gathered. Inherently, therefore, the data being studied constitute a sample of a hypothetic group technically called a "universe."

Samples can be selected with a view to adequacy in answering proposed questions. This again is a step which should be performed before a definitive study is begun. As nearly as possible, samples must be representative of the "universe," and they must be comparable in all respects other than the particular points under consideration. For instance, in order to compare the incidence of skin infections among diabetic persons with that among nondiabetic persons, it is of no use to observe hospital and office patients in the first group and all patients of private physicians in the second group. Not only is there likely to be a difference in general resistance to infection in the two groups, but one should remember that a hospital record will cover only short stated periods in a person's lifetime, whereas a physician's record may cover the patient's complete adult life, although perhaps in a less objective way. There is record of a study in which exactly this point was overlooked, and the suspicion that the incidence among the hospitalized diabetic group was artificially low for this reason is justified.[1]

Another example is an investigation to determine the disability caused by seasickness among amphibious troops and the effects of certain proposed remedies. The occupants of one

1. Williams, J. R.: Does Diabetes Mellitus Predispose the Patient to the Pyogenic Skin Infections? J. A. M. A. 118: 1357 (April 18) 1942.

boat were given a medicament, by way of prophylaxis, and, in order to equalize psychologic effects, those of another boat received a placebo. It was impossible to insure, however, that conditions in both boats would be the same, with respect to violence of motion, odors, morale, discipline and the like, each of which is conceivably a factor in motion sickness. Improvement in the comparability of samples was achieved by administration of both the remedy and the placebo in each of two boats (with due regard for the many other factors pertaining to this study which need not be described here).

Often there is no opportunity to select samples for comparability, in which event there are technics for taking into account certain points of noncomparability in interpretation of the results of a study. For example, in the comparative study of the mortality rate in two groups of premature infants, in group A 25.8 per cent died and in group B 36.4 per cent died, a mortality rate in B 40 per cent higher than in A. Investigation showed, however, that group B included a much greater proportion of infants weighing less than 1.5 Kg. than did group A. Weight is accepted as a measure of "extent of prematurity," and hence is related to the chances of an infant's dying. Calculation of rates adjusted for differences in weight distribution in the two groups revealed that adjusted mortality rates were 28.9 per cent and 28.2 per cent, respectively—identical to all intents and purposes.

Nothing has been said so far of the adequacy of samples with respect to size. This is related to the theory of probability and concerns the numbers involved, rather than the specific properties of the phenomena making up those numbers. Mastery of a mathematic technic, sometimes simple and sometimes not so simple, is all that is needed to handle this aspect of sampling and will be discussed further under "Significance Tests." The adequacy and comparability of samples in the sense referred to herein is much the more troublesome problem, and its proper consideration must be based on clinical judgment, scientific acumen, experience and plain common sense.

Measurements.—The type of observation to be made and the manner of recording are important factors in planning a survey or research problem. The use to be made of a figure determines the accuracy with which it must be observed. For example, to study the distribution of weights of school children, a reading to the nearest kilogram should be sufficiently accurate. To observe diurnal variation, in relation to certain physiologic changes, would require observation to the nearest gram or 10 Gm. unit. In general, an observation of greater accuracy is more costly, requiring more time and sometimes more expensive instruments. Accuracy beyond that which can be of conceivable use is therefore to be avoided. Caution, on the other hand, must be exercised against demanding for each measurement merely that percentage accuracy which is to be expected in the final result. If each item in the distribution depends on more than one measurement, the errors may act cumulatively instead of tending to cancel each other out, thus multiplying uncertain factors.

In recording observations, there are rules to be followed which may be common enough to the engineer or scientist but which are unfamiliar to many a clinician. For instance, 21.0 mm. means a reading of exactly 21 mm. to the nearest 0.1 mm.; 21.00 mm. is the same value, but the reading is to the nearest 0.01 mm. This is not the place to outline the science of measurements; suffice it to say that one who is to make and record instrument readings should first become familiar with standard technics of reading such instruments and reporting observations.

A warning should be sounded with regard to some common difficulties, however. In grouping numerical observations into a series of class intervals, or categories, it is necessary to have in mind exactly how the original observations were made. Let us suppose that weights of children are recorded to the nearest half-kilogram. A record of 31.5 Kg. would then represent an actual weight, which might be anywhere from 31.25 to 31.75 Kg. A record of 31.0 Kg. would represent a range of actual weights from 30.75 to 31.25 Kg. and so on. Now, if after making such records to the nearest half-kilogram, it is decided to group the observations in whole-kilogram groups, so that 31.0's and 31.5's are combined into a group labeled 31 Kg.; this covers a range of actual weights from 30.75 to 31.75 Kg. If, on the other hand, weights had been recorded to the nearest kilogram originally, 31 Kg. would represent a range of actual weights from 30.5 to 31.5 Kg. Although seemingly not a large discrepancy, if the average weights of two large groups of children, measured in different circumstances, are to be compared, a difference of 0.25 Kg. might be meaningful if real; on the other hand, it might merely be the result of different methods of recording.[2]

In recording age, an important point which is often disregarded is that years of age are commonly—but not universally—recorded as of the preceding birthday, i.e., a person is 17 years old until the day he becomes 18. When recorded to the nearest birthday, however, 17 years covers a range of actual age from 16.5 to 17.5 years (not from 17.0 to 18.0 years). In classifying a series of cases, or persons, according to age, it is highly desirable that conventional groupings be used, because comparisons with other studies by other workers are so commonly made. The briefest review of existing literature will reveal age distributions made in varying ways[3]:

Years	Years	Years	Years
(*a*) 0-4	(*b*) 0-9	(*c*) 0-10	(*d*) 0-10
5-9	10-19	11-20	10-20
10-14	20-29	21-30	20-30
15-24	30-39	31-40	30-40
25-34	40-49	41-50	40-50
35-44	etc.	etc.	etc.
etc.			

It is clear that frequencies distributed in these ways cannot be compared with each other, excepting (*d*) which is presumably the same as (*b*) if (*b*) means to the preceding birthday. Class intervals most commonly used in vital statistics are of type (*a*), sometimes combining 5-14 years into one group or maintaining 5 year intervals throughout. The latter is probably the safest rule to follow, consistent with appropriateness to the particular problem at hand.

Records.—The maintaining of records, in medicine, medical research, public health and hospitals, has become a broad field of specialization. The subject ranges from case histories consisting of several typewritten pages describing a single disease entity to punched cards where a single card contains over a hundred medical, sociologic and other facts. The type of record is determined by the use to be made of it, and again it is clearly essential that all phases of presentation and interpretation of data be considered before beginning their accumulation. Especially where large quantities of observations are to be made, failure to consider a small detail may perhaps double the cost of a survey—indeed it may on occasion even make the results valueless. An axiom which is continually being rediscovered by the researcher is that a record cannot give information on a question which was not in his mind at the time the observation was made.

There is no real substitute for experience and ingenuity in the matter of record keeping. To write a textbook on the subject would serve no purpose, because no rules could be developed to cover all types of problems. Case history forms and birth and death certificates are continually being revised on the basis of experience and new knowledge, with a proper resistance to change for the sake of uniformity. A statistical analyst of necessity becomes a specialist on records, as much as such can exist, and it is now almost inconceivable that a study of any dimensions, in medical science, can be planned without the advice of a statistician.

PRESENTATION

A scientific discussion based on quantitative data usually requires the presentation of numerical observations in one form or another. This may be as a table of original data or of calculated data, such as a frequency distribution, percentages and rates, or as a graph, a series of averages or other calculated factors. Numbers may be thought of as constituting another language, just as German or Greek, which for some readers requires translation into English and for other readers

2. The question of statistical variability of averages is of no concern at the moment and will be referred to presently.

3. Feldman, M.: Statistical Study of Life Cycle of 1,154 Cases of Duodenal Ulcer, J. A. M. A. **136**:736 (March 13) 1948.

does not, depending on the extent to which the numerical presentation is unusual or is in a conventional form presumably understandable to anyone.

The purpose of numerical expression is essentially one of economy. A case fatality rate of 10.4 per cent is a short way of stating that among the observed cases slightly more than 1 out of every 10 terminated fatally, or a manometric pressure of 120 mm. of mercury means that the pressure recorded exceeds that of the atmosphere by a stated amount, in units commonly used to measure such pressures.

In presenting a large mass of numerical data, further economy is achieved by (1) combining these into categories which can be tabulated in a logical sequence, (2) drawing a picture or graph showing the relation of observations or groups of observations to each other in a form more readily understood by the reader or (3) calculating a single number, such as an average erythrocyte count, to represent a series of cases of anemia. Individual preference of the researcher determines to some extent the type of presentation to be used and the form which tables, graphs or parameters (means, medians, standard deviations) shall take. Because of their increasingly common usage, however, conventional methods of presentation should be and are being developed.

It has been stated that the analyst should be allowed wide latitude in his manner of presentation and should not be restricted to constructing tables and graphs in a specified way. This might be satisfactory if the "translation into English" always accompanied such a presentation (as it usually should) and if the verbal explanation were always the central statement of the idea, with the table or graph a mere illustration or embellishment accompanying the story. If the latter were necessarily the case, the usefulness of tables, graphs or parameters would be restricted severely and progress in economy of presentation as well as in ease of understanding would not be possible. It is not suggested that a table or graph can supplant the text of a paper, but where the modern scientific worker must review a tremendous amount of literature in his field it would be a distinct advantage if he could obtain the meaning of a table or graph directly, without having to resort to a considerable amount of reading. (If it is argued that he should be forced to read, rather than rely solely on pictures, this can apply only to inadequate pictures—and the unscientific worker.)

Tables.—It is not proposed to set rigid standards for the construction of tables, particularly because specific standards applicable in all cases have not been, and perhaps cannot be, formulated. There are, however, certain rules which should be observed at all times, but even these cannot be outlined in complete detail here. Certain ones will be discussed, mainly as an illustration of the type of point which should be considered.

Most scientific journals pursue a necessary and desirable policy regarding typography of tables, with respect to arrangement, rulings, use of italics and so on. There are abundant instances, however, of disregard of other conventions which may, in a sense, be more important.

A table should always have a complete title, making it clear what the numbers mean. For example, instead of the heading, "Table 3—Duration," a more appropriate form would be: "Table 3—Number of Cases of Duodenal Ulcer, Distributed According to Duration, by Sex and Period of Onset (War and Prewar)." In a similar way, column headings and titles for lines of the table, should be complete enough to be self explanatory. "Group 1" as a column heading is not satisfactory, unless the title of the table defines "Group 1." [3]

Totals should be labeled and should consistently be placed either (1) at the top of a column and at the left of a row or (2) at the bottom and right. There are specific reasons for adopting one or the other of these two conventions. In (1) it may be inferred that the totals are of greater interest than the breakdown. If totals are given chiefly to assure the reader that the figures balance, (2) is preferred. Consistency, however, is desirable at all times.

In showing a column of percentages it is most important to show that the total equals 100 per cent. Table 1 illustrates the reason. In the two columns headed "Percentage," a glance at the total shows that the right hand column is a distribution of the 514 cases of anemia by age. In the first percentage column the "total" is obviously a weighted average of the five percentages. Without the convenience of the 100.0 per cent, it would be necessary to write the column headings somewhat as follows, to avoid confusion: (1) "The percentage of patients in each age group who were anemic" and (2) "The percentage of the total number of anemia patients falling in each age group." There are almost always two possible ways of calculating a series of percentages, each having its distinctive meaning.

Graphs.—In the same way that a table constitutes an orderly presentation of data, for the purpose of making their meaning more readily understood, a graph is a picture for the purpose of presenting a series of observations in the simplest, clearest manner. This general purpose is served by one or a combination of three objectives: (1) to present a picture, simply as an illustration accompanying a story, (2) to aid in an explanation which would be difficult to follow without a diagram and (3) to demonstrate facts or relationships which would not be evident without a graph. In none of these cases is the graphic presentation an end in itself but a means of demonstrating evidence supporting a stated hypothesis or conclusion.

In the first of these three objectives there is certainly no harm in expression of individuality with regard to the construction of a diagram. The picture should, among other things, be pleasing in order to attract the eye. In the latter two instances, however, the graph becomes the central theme of an exposition, with an explanatory text for the purpose of "translating into English." Hence the development of, and adherence to, certain conventions will result in clearer graphs, more readily understood, and in a decreased necessity for reliance on a laborious explanation.

TABLE 1.—*Incidence of Anemia in 1,500 Patients Admitted to Boston Floating Hospital* *

Age	Total Number of Patients	Number of Anemic Patients	(1) Percentage Anemia in Each Age Group	(2) Percentage Distribution of Anemic Patients
Under 6 mo.	237	90	38.0	17.5
6 mo. to 1 yr.	178	83	46.6	16.2
1 yr.	240	122	50.8	23.7
2-4 yr.	285	96	33.7	18.7
5 yr. and over	560	123	22.0	23.9
Total	1,500	514	34.3	100.0

* Baty, J. A.: Classification of Anemia in Infants and Children, J. A. M. A. 134: 1002 (July 19) 1947.

A complete formalization of graphic procedure, covering all possible applications, is clearly not practical. Certain general rules, however, must be followed, and a few of these may be considered as an illustration of the need for establishing conventions of some sort. Just as in connection with tables, a title should always accompany a graph, and it should be complete in describing what the diagram shows, without reference to a text. It is desirable, whenever possible, to present a table of data from which the graph is drawn. An appendix for this purpose offers a practical method of accomplishing this. Simplicity is essential; therefore separate sets of data should appear in a single graph only if they are to be compared with each other directly and not for economy of space.

Of greater importance than the appearance of a graph, however, are some basic principles regarding different types of charts adapted to portraying specific types of data. The use of lines, bars and particular scales are predicated on certain types of data, the relationship of which can be most confusing, to the analyst as well as the reader, if not properly understood. It is unfortunate that reference cannot be made to a specific textbook explaining these principles. To the writer's knowledge, there is no such single source at the present time. Our purpose can be served best in the present limited space by refer ring to the following examples: illustrating just a few of the comon points of confusion.

Figure 1[4] shows a pair of graphs as actually published recently in a medical journal. The two charts, although similar in appearance, refer to entirely different types of data. This fact is further obscured by the combined title of the figure referring to the two graphs. Figure 2 shows the same observations charted in a more appropriate way and at the same time correcting a common, though serious, error caused by the nonuniform age scale (along the horizontal axis).

In both figures, graph *A* represents a frequency distribution and graph *B* does not. In a frequency distribution, the total of all the objects observed (necropsies, in this case) is distributed over the scale of the variable (age). Since this scale is described here in nonuniform intervals, it should be drawn to show this, i. e., each year of age should be represented by a given distance on the scale, so that the age span for 4-10 years will be three times as wide as the span for age 2-4 and six times as wide as that for age 1. Constructed with this in mind, the height of each curve in figure 2, graph *A*, at any particular point, indicates the relative frequency with which cases arrive at autopsy at that particular age. This is more informative than indicating the number of necropsies in a given age group, when that age group is not comparable in width with any other age group in the distribution.

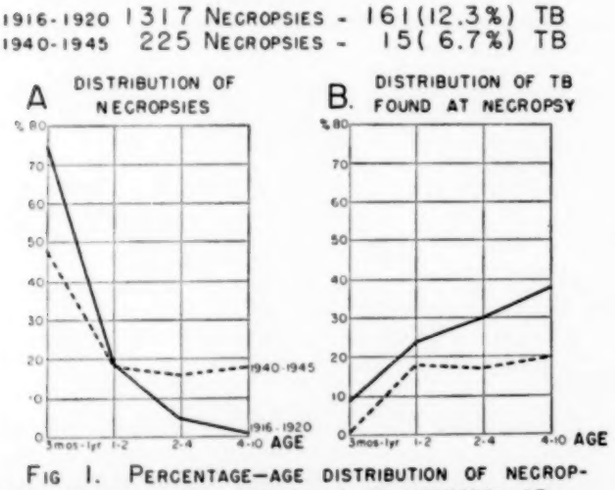

FIG 1. PERCENTAGE—AGE DISTRIBUTION OF NECROPSIES AND OF TUBERCULOSIS FOUND AT NECROPSY AT BABIES' HOSPITAL

Fig. 1.—Reproduction of a pair of graphs recently published in a medical journal.

That graph *B* (figs. 1 and 2) is not a frequency distribution is revealed by the fact that the total of the percentage figures plotted (for either of the two time periods) is not expected to add to 100 per cent. Each percentage represents a ratio of tuberculosis cases to total autopsies, calculated for a particular age group. To emphasize the different character of these percentages from the distributions in graph *A* it is highly desirable to use a different form of graph, as shown. This difference should also be made clear in the titles and scale markings of the graph. Note that the age scale has been made uniform for years, as before.

Parameters.—Parameters, or statistical constants, may be thought of as one step further in the reduction of a mass of quantitative data into a usable form. A single number, such as an average or a regression coefficient, may represent a series of observations for purposes of comparison with the corresponding parameter of another series of observations. Thus a mass of data may be arranged first as a column of numbers in a table, next as a line on a graph and then as a single statistical constant. Each form of presentation is successively more economical with respect to the symbolism used to represent large quantities of observations. But efficiency of expression is accompanied with a corresponding complexity with respect to the inherent character of the symbol. Thus an average red cell count of 5,200,000 per cubic millimeter may represent a large group of subjects. The use which can be made of this number, however, depends on many things not immediately apparent in the expression itself. It depends on the number of subjects included in the sample, the variability of the erythrocyte counts for successive subjects, the possible errors of observation, the definitions surrounding the universe sampled and so on. Consideration of these factors will be referred to presently, since they constitute the basis of problems dealing with interpretation of data. For the present it is necessary to consider briefly what some of the commonest parameters are.

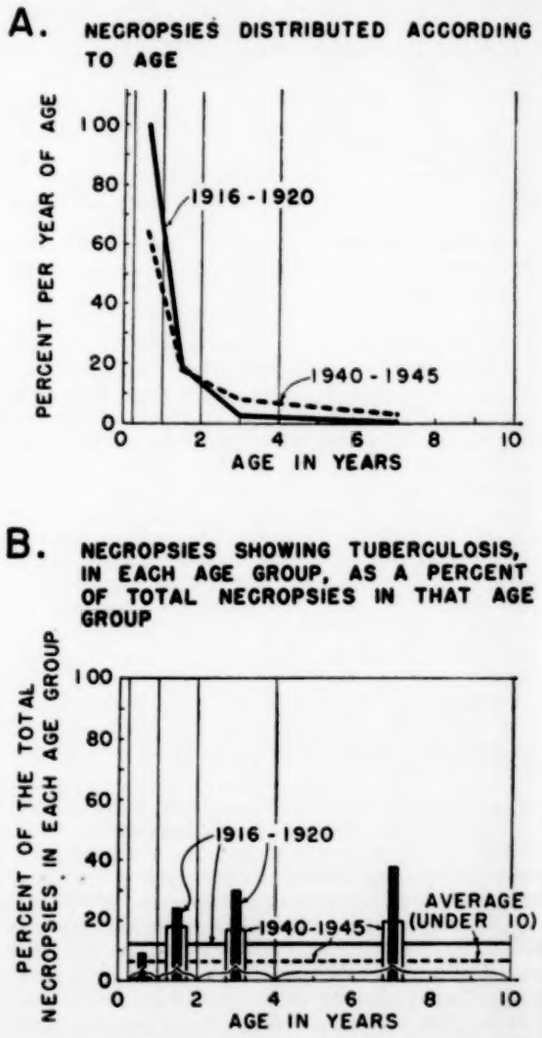

FIG. 2. TUBERCULOSIS AT NECROPSY

BABIES' HOSPITAL
1916-1920: 1317 NECROPSIES
1940-1945: 225 NECROPSIES

Fig. 2.—Graphs of the same observations as in the graphs in figure 1 charted in a more appropriate way.

Of the many types of constants which can be calculated from a group of numerical observations, two types far surpass any others in the extent to which they are used: (1) constants of central tendency, commonly called averages, and (2) constants of dispersion, or measures of spread of variability. In addition, there are coefficients related to shapes of distributions, parameters derived from analytic equations and so on. Without entering into an extended explanation, it would serve no purpose simply to describe such parameters, and the reader is

4. Medlar, E. M.: The Incidence of Pathologically Significant Tuberculosis in Routine Necropsies in Private and Public General Hospitals, New York State J. Med. 47: 582 (March 15) 1947.

therefore referred to existing textbooks on elementary statistics for a treatment of the subject. Averages and measures of spread, on the other hand, are so universally used that they cannot be dismissed without further comment.

Averages: An average is a number which represents the middle of a group of observations. Three common types are the arithmetic mean, the median and the mode. There are still others, such as the harmonic mean and the geometric mean, which are seldom encountered in medical work and may be ignored at this time.

The *mean* is the sum of all observations divided by their number. This is what is meant by the word *average* when used in ordinary conversation and is without doubt the commonest and most used parameter of the whole list. The entire theory of variability of measurements, sampling, correlation and the like is based on the use of the mean as a centering constant. The *median* is that number which divides the observations so that an equal number will lie above and below that value. The *mode* is the value which occurs more often than any other in a series of observations. In general, when numbers are symmetrically distributed, these three types of averages have the same value. It is only when observations are bunched closer to one end of their range than the other that a distinction becomes important.

Measures of Spread: Among measures of dispersion there may be as many types as there are among centering constants. Their function is to describe, in terms of the scale of the variable, the extent to which observations are spread up and down that scale. The *range* is a simple and common measure of spread, giving the interval between the lowest and highest observations in a group. Its usefulness is limited, however, because one or both of the extreme values in a series are likely to be unusual or nonrepresentative of the group.

The most important measure of spread is the *standard deviation*, also called the *root-mean-squared-deviation*. It is easily defined algebraically, and it enters into the entire theory of statistical significance more than any other parameter (except perhaps the mean). The algebraic formula [5] for the standard deviation is:

$$\sigma = \sqrt{\frac{\Sigma\,(x - m)^2}{n}}$$

which can be translated to read: the square root of the average of the squared deviations (of each observation from the mean of the group); hence the term root-mean-squared-deviation.

The meaning of the mean and standard deviation can be illustrated by considering table 2. In weighing 1,213 17 year old boys, there would obviously be a variation in weights. A single number representing the group is the mean weight of 137.6 pounds. This is useful for comparison with a mean weight for girls of 119.7 pounds. Although the average of boys is about 18 pounds heavier than the average of girls, one would not expect all boys to be heavier than all girls at this age. The spread of weight of boys is indicated by $\sigma = 20.5$ pounds. The exact relationship of σ to the total spread on the scale of weights depends on the shape of the distribution. In this case (but not in all cases) it is safe to say that the heaviest boys will be between 2 and 3 σ's above the mean, and the lightest between 2 and 3 σ's below the mean. In other words, there are undoubtedly some boys in the group who weigh as much as 180 pounds ($137.6 + 2 \times 20.5 = 178.6$) and some who weigh as little as 95 pounds ($137.6 - 2 \times 20.5 = 96.6$).

For girls σ is considerably smaller, which means that the distribution of girls on the scale of weights is not nearly as great as that for boys—these girls were more uniform in weight than the boys. In like manner, there were most likely some girls weighing as much as 145 pounds ($119.7 + 2 \times 12.3 = 144.3$) and some as little as 95 pounds ($119.7 - 2 \times 12.3 = 95.1$). Hence it would be no surprise to find small boys and girls (aged 17) of about the same weight, but it would be quite surprising to find a girl, even if well above the average weight for girls, as heavy as the heaviest boy.

5. σ = the standard deviation as measure of spread; Σ = "the summation of"; x = any particular observation; m = the mean of the observations; n = the number of observations, or sample size.

The technic of calculating the mean and standard deviation need not be discussed here. This is a matter of the proper use of a calculating machine or a slide rule. Much more important is a correct understanding of the meaning of these parameters. Applications and limitations surrounding their use will be brought out more fully in the following discussion of significance tests and statistical inference.

INTERPRETATION OF RESULTS

The matter of making scientific observations and presenting quantitative data is not new in science. It is only in recent years, however, that medical men in general have realized the need of familiarity with such technics. In the interpretation or evaluation of data, on the other hand, medical researchers are not the only ones faced with problems of analysis for which there is no set pattern. Many applications of the various theories related to probability are currently being developed in industry, finance and engineering, as well as in the biologic sciences. As a consequence, it would be impractical to expect every student of medicine to become an expert in statistical analysis. Each one should, however, have a clear basic understanding of the place where statistical analysis is of value, of the limitations of such analysis and of the philosophic principles on which statistical inference rests.

Statistical Analysis and Significance Tests.—A simple rule of thumb to determine where statistical analysis may play a part is to consider the nature of a single scientific observation related to the question under consideration. If repetition of the observation can only produce a result identical with the first, then there is no statistical problem. For example, in a study of

TABLE 2.—*Weight of Boys and Girls Aged 17 Years (at Nearest Birthday) in Iowa City (About 1934-1935)**

	Number	Weight in Pounds	
		Mean	σ
Boys	1,213	137.6	20.5
Girls	666	119.7	12.3

* Meredith, H. W.: The Rhythm of Physical Growth (in Males), University of Iowa Studies on Child Welfare, February 1935, vol. 11, no. 3; Boynton, B.: The Physical Growth of Girls, ibid., September 1936, vol. 12, no. 4.

symptoms of manifest human rabies, one of the observations recorded in each case is probably the fact of death. At present this is the only known prognosis for clinical cases, and hence there is no statistical problem involved in the question of fatality resulting from rabies. Or if barometric pressure, at a given time and place, is part of a record, that observation (for that time and place) would show no change on repetition and is hence not subject to statistical analysis.

On the other hand, if the study of rabies involves all persons exposed (not only those with manifest symptoms), there is no assurance that the record of the termination will be the same in each case. Or if, instead of barometric pressure one were recording blood pressure, a repeated observation would be likely to show some variation from the first, because of the necessarily crude method of making the observation and the natural instability of this physiologic property in man. In these cases, variability is a characteristic of the observations made. Variation constitutes the essence of a statistical problem, and it is worth noting that quantitative data not exhibiting variation of some sort are a most unusual thing.

Variation may be due to any of a number of factors: biologic variation from object to object; variation from time to time; variation due to the particular measuring instrument used; variation due to operation of the laws of chance, or variation due to inaccuracy on the part of the observer. As a general rule observed variability includes more than one, and sometimes many, of these factors. It is one of the functions of statistical analysis to analyze, or break down variability into its component parts, so that the importance of each in relation to the problem at hand may be judged.

It is axiomatic that a numerical statement has value only in comparison with some other such statement. Most commonly

one of the purposes is to formulate a conclusion as to whether or not two numbers are significantly different from each other. Today no competent research worker is ignorant of the fact that two numerical results may actually not be the same but that the difference between them may have no significance statistically. A significant difference is one which is greater than could reasonably be expected as the result of inherent variability of the original observations. It is here that a knowledge of variability, as to its cause and its magnitude, is essential.

In cases where the recorded observation is a qualitative one, such as whether a person exposed to rabies dies or not, variability enters only when a number of subjects is observed. The number or proportion who die is then the factor of interest, and variation in this number or proportion can be due to pure chance alone. The situation is analogous to the tossing of a handful of pennies: if 10 pennies are tossed, 5 may fall heads, but it is also possible to have only 4, 3, 6 or 7 heads in the result. This variability is due strictly to the inability to control the outcome for any 1 penny—or for a given subject exposed to rabies. (Whether "exposure" to rabies resulted in infection is, of course, left an open question; else the outcome might not be in doubt.) The possible magnitude of the variation due to chance alone can be calculated by a simple application of the theory of probability. All that needs to be known is the number of subjects in the sample observed and the probability of death (case fatality rate) for such subjects determined with a reasonable amount of certainty. The formula [6]

$$\sigma = \sqrt{np\,(1-p)}$$

provides a value for the standard deviation as a measure of spread to be expected on the scale representing all possible results and is analogous to the σ referred to earlier in discussing parameters.

In the case of a series of numerical observations, such as systolic pressures for a group of school children, it is the average of the group which is of interest. This average will have a variability the origin of which is a little more difficult to define. If the readings have a basic inaccuracy, a repeated set of observations may vary from the first set, with a resulting different average. Readings made by a different observer may result in still a different average. A different set of school children, identical with the first set in all general respects, will again produce a different mean systolic pressure. The average calculated for a given series of observations, therefore, has an inherent "instability," or variability. The magnitude of this variability is again most easily described by a standard deviation. In this case it is called the standard error of the mean and is given by the formula [7]

$$\sigma_m = \frac{\sigma}{\sqrt{n-1}}$$

where σ is the identical value described in discussing parameters.

A *significance test* in general consists of determining whether a given difference (standard, or root-mean-squared-deviation) is large or not, in relation to the variability inherent in the observations made. The difference may be between an observed proportion and an expected proportion (4 pennies out of 10 falling heads as compared with an expected 5 out of 10); between two observed proportions (the proportion of persons exposed to rabies dying after treatment with Pasteur's original method compared with those receiving Semple's vaccine); between an average calculated from a set of observations and an accepted normal value (the mean blood pressure for a group of school children compared with a so-called "normal"), or between two averages derived from two sets of observations (the mean blood pressure for boys compared with that for girls in the same grade). Whether or not this difference is significant is determined by the magnitude of differences which could easily arise because of "chance," or uncontrolled variability, alone. The observed difference is commonly designated as x and the magnitude of differences to be expected due to normal variation is measured by σ_x, which can be calculated by the formula:

$$\sigma_x = \sqrt{\sigma_1^2 + \sigma_2^2}$$

where σ_1 and σ_2 are the measures of variability (standard errors of the mean) for the two samples in question, as described previously. (This formula assumes that the samples are independent, i. e., uncorrelated. If that assumption is not valid, the formula will not suffice.)

The ratio x/σ_x will generally be less than 2.5 when the difference is due to random factors, or "chance," only. Therefore, if x/σ_x is less than 2.5 one must conclude that the observed difference could have been the result of random sampling alone, and one has no evidence that it was due to whatever factor is under consideration, e. g., the type of vaccine used, or the sex of the school children.

The x/σ test has been referred to here in the most general terms, and it is not my purpose to explain the technic of its calculation. Other names commonly connected with the same procedure are "t test," "relative deviate" and "critical ratio"; these sometimes have a slightly modified meaning. Other tests of significance are the χ^2 (chi-squared) test, the point binomial, analysis of variance and so on. Representing different technics, applicable in prescribed circumstances, they are nevertheless based on the same general principle, viz., that of comparing observed differences with expected variability due to chance or other uncontrolled factors.

TABLE 3.—*The Probability (P) of Obtaining a Difference as Great as or Greater Than x, Due to "Chance" Alone, When x/σ Is as Given*

$\frac{x}{\sigma}$	P	$\frac{x}{\sigma}$	P	$\frac{x}{\sigma}$	P
0.0	1.000	2.0	0.046	4.0	0.00,006
		2.1	0.036		
1.0	0.317	2.2	0.028	5.0	0.00,000,06
		2.3	0.021		
1.5	0.134	2.4	0.016	6.0	0.00,000,000,2
		2.5	0.012		
1.9	0.057	2.6	0.009	∞	0
		2.7	0.007		
		2.8	0.005		
		2.9	0.004		
		3.0	0.003		

Of greatest importance for consideration at the present time are not the specific technics of the different tests, nor the exact type of problem to be solved by each, but the limitations surrounding significance tests in general and the underlying principles of statistical inference.

Statistical Inference and the Limitations of Significance Tests.—Ideally, one might wish to use statistical data to prove the value of a given form of therapy or to prove the relationship between two characteristics, such as body weight and basal metabolic rate. Proof, in the strictest sense however, is not obtainable from data merely by virtue of their being in numerical form. Indeed, because of the very character of statistical observations, their inherent variability and their strict limitations in application to the problem at hand, they can do no more than lend support, or fail to lend support, to a given hypothesis arrived at on purely logical grounds. As evidence, they can be strong or weak or in-between. The strength or weakness of such evidence is described by *confidence levels*, which in turn can be given in terms of a percentage scale: 100 per cent confidence is equal to certainty; 50 per cent confidence means equal likelihood that the hypothesis is actually correct or that the hypothesis appears to be supported by the evidence purely as a result of random variability. Obviously, a relatively high degree of confidence must be achieved—95 or 99 per cent—to provide evidence which actually does support the hypothesis in question.

6. σ = the standard deviation of the probability distribution; n = the number of objects in the sample, or sample size; p = the probability of the event in question occurring (expressed as a fraction, the number of positive occurrences divided by the total of positive and negative occurrences).

7. σ_m = the standard error of the mean; σ = the standard deviation of the observed distribution; n = the number of subjects observed, or sample size.

This percentage scale to describe the level of confidence may be understood more readily by considering the complementary scale, which then represents "the chances of being wrong." Certainty means there is 0 chance of being wrong, and a reasonably high level of confidence is defined as 1 per cent or 5 per cent chance of being wrong. The latter percentage is now analogous to (sometimes, though not necessarily, identical with) the *probability* of obtaining the observed results due to random variation, or "chance," alone. This probability value, commonly designated by the letter P, is the accepted criterion for determining significance in practically all significance tests. In the case of the x/σ test, the theory of probability, with its relation to the "normal probability curve," gives specified P values for each x/σ value, as shown in table 3.

It was mentioned earlier that when a difference (x) is actually due to nothing but chance, x/σ is not likely to exceed 2.5. From table 3 it can be seen that the probability (P) of its exceeding 2.5 is about 0.01, or 1 chance in 100, which is considered unusual or unlikely. From this it is argued that when x/σ is greater than 2.5, the cause of the observed difference (x) must have been something other than chance. The conclusion is justified on the grounds that, as the probabilities indicate, one would be wrong only once in a 100 such decisions, which is equivalent to 99 per cent confidence. If 95 per cent confidence is sufficient, that means one can risk being wrong 5 per cent of the time, and for $P = .05$, one sees that x/σ is about 2.0, which for some purposes is considered to be a satisfactory minimum for the significance ratio. On the other hand, it is also possible that confidence equal to near certainty is required. This is represented by a value of P approaching 0 corresponding to $x/\sigma = 3$, 4, or a greater value. It may be noted that $P = 0$ only when variability of observations is no longer a factor, and it will be recalled that in the original premise this did not constitute a statistical problem. Hence the assertion that, when there is a variability of any kind in the original observations, proof positive is not possible, because 100 per cent certainty, corresponding to $P = 0$, is never reached.

For an example, let us refer again to table 2, showing mean weights of boys and girls. The difference between the mean is

$$x = 137.6 - 119.7 = 17.9 \text{ pounds}$$

σ_x is given by the formula $\sigma_x = \sqrt{\sigma_{m_1}^2 + \sigma_{m_2}^2}$

where σ_{m_1} and σ_{m_2} are the standard errors of each of the means, calculated as follows:

$$\sigma_m = \frac{\sigma}{\sqrt{n-1}}$$

Hence $$\sigma_{m_1} = \frac{20.5}{\sqrt{1212}} = 0.589 \text{ pound}$$

and $$\sigma_{m_2} = \frac{12.3}{\sqrt{665}} = 0.477 \text{ pound}$$

$$\sigma_x = \sqrt{(.589)^2 + (.477)^2} = 0.758 \text{ pound}$$

$$\frac{x}{\sigma_x} = \frac{17.9}{.758} = 23.6$$

This is an exceedingly large value of x/σ, as was to be expected. There is no doubt that the difference in weight between boys and girls aged 17 years is greater than could possibly be accounted for by random variation in weight measurements. The value of P associated with $x/\sigma = 23.6$ is so close to 0 that the degree of certainty attained is to all intents and purposes perfect. In order to understand the implications of a significance test, however, it must be remembered that the conclusion is based on a mathematic procedure and that in theory there is a chance (1 in many, many billions perhaps) of obtaining such a difference as the result of random variations—and hence of being wrong in our conclusion.

In the case of weights of boys and girls, the lack of doubt as to the significance of the difference is based largely on the knowledge of physiology and growth as related to sex, and a significance test was hardly necessary. In other instances, however, empiric knowledge may not be at hand. Statistical significance then carries the burden of evidence, and its limitations must be understood.

When a difference is not significant, it can only mean that chance variations could have produced a difference as large as the one observed. There is nothing to indicate that chance alone did produce that difference. To say that a nonsignificant difference is not real is therefore a distinct error.

The preceding example is a case of a highly significant difference, with the conclusion that the evidence is good in supporting the hypothesis that boys are heavier than girls. In the case where an observed difference turns out to be not significant, the conclusions to be drawn are more complex, and it is here that errors in interpretation are commonly made. An example will provide the best means of explaining the inferences and limitations pertaining to such a situation.

Let us suppose that the mean systolic pressure for a group of Negro soldiers is to be compared with the mean systolic pressure for a comparable group of white soldiers. The two means are not identical, but a significance test shows that the difference between them is no larger than could easily have occurred as the result of random variability only. Clearly one then has no evidence that there is any difference between Negroes and white persons in this respect. Can one now say, "There is no difference between the two races as regards systolic pressure?" One most decidedly cannot. The significance test itself is based on a "null hypothesis," which states the question in this form: "On the hypothesis that there is no difference between mean systolic pressure in white persons and in Negroes, could a difference as large as the one observed be the result of random variation?" Having answered this question in the affirmative, there is no further evidence whatsoever in these data, that the two races have essentially the same blood pressure.

The significance test is limited strictly to the mathematic behavior of numbers—the numbers in this case being certain sphygmomanometer readings. The lack of evidence of an association between race and blood pressure is not evidence of lack of such an association. On this point there must be no doubt.

COMMENT

Within the space of these pages it has been possible to do no more than touch on one type of significance test, as an example of the purpose and limitations of statistical inference. To cover the multitude of problems and applications in this field would constitute a short course in probability and statistical analysis. The research worker in medicine, as well as in other sciences, can hardly be considered competent without some such training. Even so, more often than not the services of an expert in this field are essential, and it is our aim to point out the need rather than to explain the function of such application.

Whenever quantitative data play a part in a piece of research, the experimental design as well as the statistical analysis cannot receive too much emphasis, before, during and on completion of the project. Adequate recording and clear presentation, to achieve the maximum results from any piece of research, are equally important. But the research analyst cannot rest with the mere observation of phenomena and their presentation. He inevitably assumes a certain responsibility for the interpretations to be placed on his findings and the use to be made of his contribution to science.

Most important of all, however, is for the reader of medical and scientific literature, the medical "common man," to have an appreciation of the need for, and the purposes of, proper presentation and analysis. The student of medicine must have some knowledge of technics of handling quantitative data (1) in order to understand a correct presentation and (2) in order to form a judgment (or at least entertain a healthy suspicion) as to whether a given exposition or analysis is adequate or not.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET - - - CHICAGO 10, ILL.

Edited by
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Subscription price - - - - Twelve dollars per annum in advance

Cable Address - - - - "Medic, Chicago"

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SATURDAY, SEPTEMBER 17, 1949

THE "VERTICAL" TRANSMISSION OF CANCER

The suggestion that cancer is caused by viruses transmitted "vertically" from one generation to another is made by L. Gross [1] of the Veterans Administration Hospital, New York. Mammary carcinoma of mice is caused by a filterable agent which is transmitted through the milk of nursing females.[2] This agent is destroyed by heating to 61 C. for thirty minutes [3] and can be neutralized by a specific immune serum.[4] The development of mammary carcinoma in mice can be prevented by simply isolating newly born animals from their potentially cancerous mothers and transferring them for nursing to mice whose milk is free from the tumor agent. The newly born mice become infected by the milk of their mothers; they remain in perfect health, however, through early adult life, mammary carcinoma developing at 1 to 1½ years of age. In the meantime, they may transfer the tumor agent to their own offspring and thus assure the continuation of the disease. In other words, breast cancer of mice is claimed to be a communicable disease.

The natural transmission of mammary carcinoma in mice is different from that in the common communicable diseases. A mouse carrying the tumor agent can be placed in the same cage with healthy, susceptible mice; yet transmission of the disease will not result. The same mouse, however, will transmit the tumor agent through milk to her own daughters and through these to granddaughters, great granddaughters, and onward. This pattern of transmission may be designated a "vertical epidemic." [1] The pattern of "vertical" transmission of pathogenic agents is not limited to the virus of mammary carcinoma of the mouse, but is also followed by many other parasites, particularly in plants and in insects.

Gross [1] assumes that breast cancer in other mammals, including man, may be caused by agents similar to that responsible for mammary carcinoma of the mouse. If this is true, women with a history of cancer should not nurse their babies; artificial feeding should be substituted. This simple measure may interrupt the flow of the virus and eradicate a strain of human breast cancer within one generation. Gross advances the following working hypothesis: There may exist a group of transmissible agents causing different kinds of tumors. A most striking feature of these agents would be their faculty to pass "vertically" from one host to another of successive generations, through the ovum, or sperm, or through the mother's milk. During a long asymptomatic phase the infected hosts would appear perfect in health, but harbor the virus and transmit it to succeeding generations. The activation of the hitherto latent agent in the transmitting host would then occasionally follow.

Once activated, the tumor virus would cause at the site of activation a rapid growth of cells with infiltration of the surrounding tissue, and later spread through the lymphatics, and possibly through the blood. In many instances, however, the tumor virus might not become activated; there would be no symptoms of tumors in such hosts even though they might transmit the virus; the virus would appear to have "skipped" an intermediary host. Since the virus would be transmitted only from one host to another of successive generations, each "skipping" of an intermediate host would result in the "skipping" of an entire generation; the "skipping" of two successive hosts would result in "skipping" of two generations. Tracing the course of the virus may become extremely difficult. Accurate and complete records covering many successive generations may be needed for this purpose. Gross assumes that, should such records become available, each case of human cancer could then be traced to another case of cancer in one of the patient's ancestors.

The "vertical epidemic" theory differs from other current theories on the virus origin of cancer by the introduction of the concept of a "vertical"—i. e. generation to generation—transmission of the virus and by the assumption that the virus may be dormant and transmissible as well as active and tumor forming. This hypothesis is not perfect, however. Why do tumors develop in animals submitted to prolonged irradiation with roentgen rays or radium? Why can tumors be produced almost at will, at least in mice, by the application of many carcinogenic chemicals? Is it possible that all these animals are carriers of an inactive tumor virus which is being activated by the

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2. Bittner, J. J.: Some Possible Effects of Nursing on the Mammary Gland Tumor Incidence in Mice, Science **84**: 162, 1936; Breast Cancer in Mice as Influenced by Nursing, J. Nat. Cancer Inst. **1**: 155, 1940.
3. Andervont, H. B., and Bryan, W. R.: Properties of the Mouse Mammary Tumor Agent, J. Nat. Cancer Inst. **5**: 143, 1944.
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carcinogenic agent? Gross [1] stresses that, in the mouse at least, hormonal stimuli will prompt the development of breast cancer in male mice otherwise free from cancer only if the mammary carcinoma virus is present in the host.[5] If this is true for other carcinogenic factors the assumption is necessary that the tumor virus or viruses are so widely spread in the animal kingdom that most individuals carry one or another of them in their cells without, in most instances, showing any tumors.

The "vertical epidemic" theory of cancer merits careful consideration because it raises the question of preventing breast cancer in women by the artificial feeding of infants born to mothers with a family history of cancer.

EPIDEMIC PLEURODYNIA

Finsen in 1856 reported outbreaks of an epidemic disease in Iceland characterized by muscular rheumatism of the chest or "pleurodynia." Daae and Homann in 1872 reported similar attacks in Norway and provided the first careful description. In 1930, Sylvest studied the disease on the Danish island of Bornholm, where the disease appeared to be endemic. The disease was made reportable in Denmark, and some 10,000 cases were reported in the next two years. Since then many epidemics have been described in Scandinavian countries and in the British Isles. The disease was first reported in the United States in 1888 by Dabney, who gave an account of an epidemic in Virginia. The syndrome has been variously designated as Bornholm disease, epidemic muscular rheumatism, acute benign dry pleurisy, epidemic pleuritic pain, Balme disease and "devil's grip." Tasker Howard and associates [1] reported an outbreak of the disease with 166 cases in Brooklyn in the summer of 1942. Scadding [2] described an acute febrile illness characterized by symptoms and signs suggesting dry basal and diaphragmatic pleurisy in a British military hospital in the Suez Canal. The most recent report is that of Finn and co-workers [3] on an outbreak in Brookline, Mass., during the late summer and early fall of 1947. One hundred and fourteen patients were admitted to the Boston City Hospital. The symptoms observed were much like those reported in the previous outbreaks. The clinical picture was characterized by an abrupt onset of a severe pain at the costal margins, the abdomen or the shoulder. The typical severe pleuritic type of pain was described variously as "smothering," "stabbing," "knifelike" and "like a vise around the lower ribs." The pain was aggravated by deep breathing, yawning, coughing and body movements. Pleuritic friction rub, cutaneous hyperesthesia, abdominal tenderness and rigidity were less frequently observed. The duration of the pain was from two days to seven days. Slight rise in leukocytes present during the first two or three days was invariably followed by definite leukopenia. Spinal fluid in patients with symptoms of central nervous system involvement frequently showed increased albumin content and definite pleocytosis. Roentgenologic studies revealed normal lung fields and freely movable diaphragm. Tasker Howard,[1] McConnell [4] and Gsell [5] reported symptoms of meningoencephalitis in some of their patients. Other complications observed were orchitis and, rarely, pericarditis.

These outbreaks were, no doubt, due to infection, as suggested by their occurrence in epidemics with a similar febrile course and by the evidence of direct case to case transmission. The failure to demonstrate any constantly present bacterial agent and the occurrence in some cases of benign serous meningitis or meningoencephalitis and orchitis suggest that infection is caused by a virus. Finn and co-workers [3] state that blood cultures taken at various times during the first ten days of the illness did not contain pathogens. Cultures from the throat did not reveal a predominant organism. Studies for the presence of heterophile antibodies were likewise negative. Intra-amniotic inoculations on eggs with throat washings, cerebrospinal fluid and rectal swabs collected from typical patients during the acute phase of illness gave negative results as to the presence of a virus.

The treatment, largely symptomatic, included rest in bed and the use of analgesics. Penicillin and streptomycin appeared to be without special value.

HIATUS HERNIA

Roentgenologic studies during two decades have demonstrated that hernia of the esophageal hiatus, once considered rare, is not infrequent. Brick [1] notes that there were 308 hiatus hernias among 3,448 patients subjected to routine barium study of the upper part of the gastrointestinal tract during the years 1945 and 1946 in the Boston City Hospital. Ritvo [2] pointed out in 1930 that the roentgenologic examination is the only means of arriving at the diagnosis of hiatus hernia, but that the patient must be studied in the prone, supine and oblique positions, since hiatus hernia is only rarely seen with the patient erect. Ritvo [2] reported 60 cases of hiatus hernia, all diagnosed during routine roentgenologic examination of the stomach with the opaque

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meal. These occurred during a period in which about 8,000 cases of gastrointestinal disease were studied roentgenologically. According to Schnepp [3] diaphragmatic hernia was noted in 0.02 to 8 per cent of consecutive routine gastrointestinal roentgenologic examinations by various observers. Kirklin and Hodgson [4] reported 306 instances of hiatus hernia diagnosed roentgenologically at the Mayo Clinic in one year. Esophageal hernia was the most common type of diaphragmatic hernia. Among these 306 cases, 31 were of "short" esophagus type and an additional 51 of shortened esophagus.

The etiologic factors which contribute to the development of hiatus hernia are congenital defects in the diaphragm, age, sex, obesity and pregnancy. The majority of the cases are seen in patients past 40 years of age, with the greatest frequency between 60 and 80 years. The condition is almost twice as frequent in women as in men and is most frequent in women who have borne children. Obesity appears to be an important predisposing factor.

The symptoms, according to Kirklin and Hodgson,[4] depend on three factors: (1) the mechanical interference with herniated viscera; (2) interference with function of the diaphragm, and (3) the amount of increased pressure within the thorax. The most frequent symptom is substernal pain. Other symptoms are heartburn, nausea, vomiting, regurgitation and constipation. The symptoms frequently are indefinite and mild, and of years' duration. Bleeding, which occurs in a certain number of cases, is due to erosion and ulceration of gastric mucosa within the hernia. The erosion and ulceration are due to chronic or recurrent venous congestion caused by pressure exerted by the margins of hernia on the vascular supply. Radloff and King [5] observed 50 cases of esophageal hernia at the Mason Clinic during the period from 1944 to 1946. They stress particularly the frequent association of other pathologic conditions with hiatus hernia. In their material only 30 per cent had symptoms which could be attributed directly to the hernia. In 68 per cent, concomitant disease was present and was responsible for the symptoms. In Brick's [1] series roentgenologic signs of an associated gastrointestinal lesion were observed in 20 per cent of the cases. The most frequent associated lesion was a duodenal ulcer.

In the series reported by Jankelson and Morein,[6] ulcers of the stomach and duodenum accompanied hiatus hernia in 25 per cent of the cases. In Brick's [1] material there were 31 duodenal ulcers, or an incidence rate of 10 per cent. Among other complications are mentioned esophageal ulcers and an ulcer niche within the herniated portion. Cancer of the esophagus or stomach in combination with a hiatus hernia is unusual. Chronic cholecystitis and cholelithiasis were reported in 14 per cent of cases by Wilkinson, in 15 per cent by Polley and in 17 per cent by Jones.

Hiatus hernia, regardless of its size, may be completely asymptomatic and may be demonstrated only accidentally. Radloff and King [5] stress that most important in the treatment of diaphragmatic hernia are correction of the coexisting disease, securing a reduction in weight and treatment of the underlying emotional factors. Surgical intervention is indicated when the symptoms are found to be due directly to the hernia and are not relieved by conservative measures.

3. Schnepp, K. H.: Diaphragmatic Hernia: Its Incidence and Treatment, Illinois M. J. **83**: 404-411 (June) 1943.

4. Kirklin, B. R., and Hodgson, J. R.: Roentgenologic Characteristics of Diaphragmatic Hernia, Am. J. Roentgenol. **58**: 77-101 (July) 1947.

5. Radloff, F. F., and King, R. L.: Esophageal Hiatus Hernia, Gastroenterology **9**: 249-252 (Sept.) 1947.

6. Jankelson, I. R., and Morein, S.: Complications of Diaphragmatic Hernia, Rev. Gastroenterol. **7**: 134 (March-April) 1940.

Current Comment

ANNUAL REPORT OF THE PUBLIC HEALTH SERVICE

Ten years ago the Annual Report of the Public Health Service used to be received in the headquarters of the American Medical Association some six months after the end of the fiscal year. On Sept. 6, 1949, the Annual Report of the Federal Security Agency, Public Health Service, for the fiscal year ending June 30, 1948, was received. This report is now fourteen months old; although it contains information of great importance to the nation, much of it is already stale news. Facts mentioned in the report of Q fever studies (page 311) long ago appeared in the newspapers, and some of them have already been modified by later studies. The fact that experimental Q fever vaccine is available for distribution for experimental use should have been given more prompt and wider publicity than this report provides. Announcement now of the amount of spotted fever vaccine distributed from the Rocky Mountain laboratory is misleading, as this laboratory has discontinued distribution of this vaccine. The scope of the work of the U. S. Public Health Service has continually broadened and now embraces many activities that were not even considered ten years ago as suitable work for the Public Health Service. One million dollars was appropriated to demonstrate use of sodium fluoride for prevention of dental decay. Research activities are carried on in the National Heart Institute, the National Dental Research Institute, the National Cancer Institute and the National Mental Health Institute. The new clinical and laboratory research center at Bethesda has $40,000,000 for construction. Our country's share of the expense of the World Health Organization is $1,900,000; we send about 25 persons to Europe for the meetings. The funds appropriated for the Public Health Service have increased to nearly fifteen times the amount appropriated ten years ago. The total appropriations for the fiscal year 1938 were $13,146,980, and for the fiscal year 1948 they were $192,848,100.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

Sept. 12, 1949.

Brookings Institution Launches Broad Health Survey

The Brookings Institution of Washington has confirmed a report, first published in the Washington Report on the Medical Sciences, that it has launched a comprehensive survey of medical care in the United States. The study, which it is estimated will take about two years, will examine the facts and figures of private medical practice, voluntary prepayment systems, insurance indemnity coverage, hospital facilities, industrial health protection and all other major aspects of the problem. Observations will be published in two volumes, one on availability of services and the other on evaluation, according to present plans.

Funds for Military to Employ Civilian Doctors

Medical department appropriations for Army, Navy and Air Force in 1950 could be used, when necessary, for employment of civilian physicians, dentists and nurses, by provisions of the military appropriations bill in the form in which it has passed the Senate. The authorization was inserted at the request of the Army, which wishes to be allowed to engage civilians in the event its roster of uniformed medical practitioners falls short of needs.

The authorizing amendment, which is expected to be approved by the House, grants funds "for the employment of such additional civilian physicians, dentists and nurses as may be required for the direct care and treatment of patients." Professional personnel so employed would be engaged, graded and compensated on the same basis as in the Veterans Administration.

Congressional Health Study Itinerary Disclosed

The House Interstate and Foreign Commerce Committee has made public the European itinerary of its members, who are spending the middle and latter part of September studying governmental medical care plans in England and on the Continent. Five members embarked on September 3: Representatives Crosser, Beckworth, Ellsworth, Bennett and Gillette. The others were scheduled to leave Washington September 10 by military air transport. Their itinerary gives them five days in the British Isles, three days in Sweden, one day each in Germany and Switzerland, two days in Rome, Italy, and two days in Paris, France. Arrival time in Washington is scheduled for September 26.

Representative Miller Attacks Socialized Medicine

In a twenty minute speech on the House floor August 22, Representative A. L. Miller (R. Neb.) assailed the "agitation in this country for compulsory health insurance which stems from the President and his busy little group of planners who are determined to make the United States a welfare state." He charged that such a program would entail enormous cost, bring about a "political pill mill," reduce professional standards and nullify gains that have been made in improving the nation's health.

Creation of Two New Research Institutes Approved

A National Institute on Rheumatism, Arthritis and Metabolic Diseases and a separate National Institute on Neurological Diseases and Blindness would be established in Public Health Service under provisions of a bill approved August 25 by the Senate Labor Subcommittee on Health Legislation. The measure (S. 1651, as amended) also would give the Surgeon General discretionary authority to set up other special institutes whenever such action is indicated.

Although Dr. Leonard A. Scheele, Surgeon General, had previously testified before Senate and House committees that he was opposed to establishment of more special disease institutes by congressional mandate, the manner in which S. 1651 has been amended makes the bill acceptable to the Public Health Service and the Federal Security Agency.

On August 23, the Senate Labor and Public Welfare Committee favorably reported S. 1706, authorizing admittance into Public Health Service hospitals of certain persons committed by state courts; S. 2227, amending the act of July 18, 1940, on conditions governing admissibility of Virgin Islanders into St. Elizabeths Hospital in Washington, and S. 2228, authorizing disposal of venereal disease rapid treatment facilities by the Public Health Service. Previously the three bills had been approved by the Murray subcommittee on health legislation.

Heart Grants of $8,614,737 Announced

Eighty-five medical schools, hospitals and research institutions in thirty-four states and the District of Columbia are beneficiaries of federal grants aggregating $8,614,737 for research, teaching and construction assistance in the field of heart disease. The awards, announced by Federal Security Administrator Oscar R. Ewing, are exclusive of $1,200,000 allocated in July for continuing heart research projects already under way.

Assistance in construction of laboratory and clinical facilities at twenty-two nonfederal institutions accounts for $5,890,395 of the grants. The next largest amount—$2,053,310—is for one hundred and eighty-nine research projects at sixty-six institutions. The remaining $671,032 will be divided among forty-six medical schools for the purpose of improving instruction in cardiovascular diseases.

Functions of New Federal Medical Unit Defined

Dr. Leonard A. Scheele, Surgeon General, has signed an order establishing and defining the responsibilities of a new unit in the U. S. Public Health Service. It is the Division of Medical and Hospital Resources, a component of the Bureau of Medical Services in the health service. Its creation, according to the Surgeon General's office, is in "recognition of the need for the development and promotion of methods, standards and procedures for the practical provision of medical, hospital and related services in order to assure progress in the preservation of the health of the American people."

The division will conduct research and provide advice on broad questions of national policy in hospital and related care; formulate hospital and related care programs and operational plans; give technical aid to other parts of the U. S. Public Health Service; develop and promote standards and technics for practical provision of hospital and allied services, including training of personnel, specialization and use of facilities; develop guides and consultative services in such specialties as medical-record-keeping, administrative practices and outpatient services, as well as in the broad fields of medicine, surgery, dentistry and nursing, and conduct medical-economic and social-economic studies.

The division will have four branches—medical economics, medical-hospital administration, clinical services and program operations—and a professional reference service.

Progress Made Toward Industrial Health Body

At the conclusion of a meeting in Washington on September 8, Dr. C. M. Peterson, secretary of the Council on Industrial Health of the American Medical Association, announced that encouraging progress has been made toward formation of a permanent conference which would bring cooperative effort to bear on advancement of health and safety in industry. Attending the September 8 meeting at the Hotel Statler were B. B. Lausche, E. H. Robertson and A. L. Kirkpatrick, representing the U. S. Chamber of Commerce; Collins Winston, National Association of Manufacturers; Harry Reed, Congress of Industrial Organizations; Dr. A. J. Lanza, chairman of the Council on Industrial Health; Dr. Raymond Hussey, and Dr. C. M. Peterson. Final organization plans are expected to be completed at the group's next meeting here, probably in October.

Local Public Health Units Bill Passed

Completion of congressional action on legislation to strengthen and expand local public health services through federal support awaits resumption of business by the House September 21. The Senate passed the bill (S. 522) on August 28, substantially in the form in which it was favorably reported two weeks earlier by Senator Lister Hill (Dem., Alabama). One amendment made on the Senate floor prior to passage provides that industrial accident prevention shall not be included among public health services in the meaning and intent of the proposed law.

Modified Bill Introduced on VA Doctors' Salaries

In the midst of public hearings, conducted by the House Veterans Affairs Committee, on legislation to increase salaries of physicians, dentists and nurses in the Veterans Administration's department of medicine and surgery, a substitute bill was introduced for the purpose of incorporating certain technical points suggested by VA. This new measure, H.R. 6022, replaces H.R. 5324. The sponsor is the same, namely, Representative A. Leonard Allen (D., La.).

New Appointments Made to AEC Biology-Medicine Division

Two new appointments to the medical branch of the Biology and Medicine Division, Atomic Energy Commissions, were announced September 1. At the same time an acting chief of the division's biology branch was named.

Dr. Charles Little Dunham and Dr. George A. Hardie have been assigned to the Washington main office of the medical branch. The former was assistant professor of medicine at the University of Chicago in charge of the arthritis clinic and hospital service, while Dr. Hardie formerly was a fellow in the Department of Medicine at Johns Hopkins University.

Appointed acting chief of the biology branch was Dr. Paul B. Pearson, who joined the commission staff earlier this year from Texas Agricultural and Mechanical College, where he was head of the department of biochemistry and nutrition and served as dean of the graduate school. He succeeds Dr. James H. Jensen, whose resignation became effective September 1.

Office of Education Report Cites School Health Services

According to a report issued September 11 by the Office of Education (Federal Security Agency), nearly 5,000,000 children between the ages of 5 and 14 live in counties lacking organized medical service in public elementary schools. Thirty to 49 per cent of the children in ten states live in counties without school health services, and in ten other states at least one half of the children are in a similar situation, according to the report. It also pointed out that during the past year, of a total of 368,000 degrees granted by colleges and universities, only 5,200 were awarded in medicine, 1,700 in dentistry and 3,500 in nursing.

Woman's Auxiliary

CONNECTICUT CHILD HEALTH CONFERENCE

The Woman's Auxiliary to the Connecticut State Medical Society will sponsor a Community Child Health Conference September 21 at the Centinol Hill Hall in Hartford. Co-sponsoring organizations and agencies include the Parent-Teacher Association of Connecticut, the State Department of Health, State Department of Education and the Connecticut State Dental Association. The morning session of the conference will be devoted to discussions on child health needs in Connecticut's communities and the afternoon session to resources available for child health and their effective use in the community. Thomas A. Hendricks, secretary of the Council on Medical Service, American Medical Association, Chicago, will speak on "Community Health Leadership!" Attendance at the conference will include representatives from school districts, parent-teacher associations and community service clubs, local health officers and town officials.

Coming Medical Meetings

Annual Conference of State Secretaries and Editors, Chicago, A. M. A. Building, Nov. 3-4. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

Ambulatory Fracture Association, Toronto, Canada, Royal York Hotel, Oct. 24-27. Dr. H. W. Wellmerling, 120 S. LaSalle St., Chicago 3, Secretary.

American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 9-14. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.

American Clinical and Climatological Association, White Sulphur Springs, W. Va., The Greenbrier, Oct. 27-29. Dr. James Bordley III, Bassett Hospital, Cooperstown, N. Y., Secretary.

American College of Surgeons, Chicago, Stevens Hotel, Oct. 17-21. Dr. Paul B. Magnuson, 40 E. Erie St., Chicago 11, Secretary.

American Hospital Association, Cleveland, Sept. 26-29. Mr. George P. Bugbee, 18 East Division St., Chicago, Executive Secretary.

American Public Health Association, New York, Oct. 24-28. Dr. Reginald M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

American Roentgen Ray Society, Cincinnati, Oct. 4-7. Dr. H. Dabney Kerr, University Hospitals, Iowa City, Iowa, Secretary.

American Society for the Study of Arteriosclerosis, Chicago, Hotel Knickerbocker, Nov. 5-7. Dr. O. J. Pollak, Quincy City Hospital, Quincy 69, Mass., Secretary.

American Society of Clinical Pathologists, Chicago, Drake Hotel, Oct. 11-15. Dr. C. G. Culbertson, 740 S. Alabama St., Indianapolis, Secretary.

American Society of Tropical Medicine, Memphis, Tenn., Nov. 6-9. Dr. Frederick J. Brady, National Institute of Health, Bethesda 14, Md., Secretary.

Association of Military Surgeons of the United States, Washington, D. C., Nov. 10-12. Col. James M. Phalen, Army Institute of Pathology, Washington 25, D. C., Secretary.

Central Society for Clinical Research, Chicago, Drake Hotel, Nov. 4-5. Dr. Kenneth G. Kohlstaedt, 960 Locke St., Indianapolis 7, Secretary.

Colorado State Medical Society, Denver, Shirley-Savoy Hotel, Sept. 20-23. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver, Executive Secretary.

Conference of State and Provincial Health Authorities of North America, New York, Oct. 28. Dr. Russell O. Saxvik, State Health Officer, Bismarck, N. D., Secretary.

Delaware, Medical Society of, Wilmington, Oct. 10-12. Dr. W. Edwin Bird, 822 North American Bldg., Wilmington, Executive Secretary.

District of Columbia, Medical Society of the, Washington, Hotel Statler, Oct. 17-19. Mr. Theodore Wiprud, 1718 M St. N.W., Washington 6, Secretary.

Gulf Coast Clinical Society, Pensacola, Fla., Oct. 6-7. Dr. Arthur J. Butt Jr., 1101 N. Palafox St., Pensacola, Fla., Secretary.

Indiana State Medical Association, Indianapolis, Sept. 26-29. Mr. Ray E. Smith, 1021 Hume-Mansur Bldg., Indianapolis 4, Executive Secretary.

Inter-American Congress of Surgery, Chicago, John B. Murphy Memorial Auditorium, Oct. 21-23. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Chairman Program Committee.

International College of Surgeons, United States Chapter, Atlantic City, Haddon Hall, Nov. 7-12. Dr. Arnold S. Jackson, 1516 Lake Shore Drive, Chicago 10, Secretary.

Inter-State Post Graduate Medical Association of North America (International Medical Assembly), Philadelphia, Oct. 31-Nov. 3. Dr. Tom B. Throckmorton, Equitable Bldg., Des Moines, Iowa, Secretary.

Kansas City Southwest Clinical Society, Kansas City, Mo., Municipal Auditorium, Oct. 3-6. Dr. W. Merritt Ketchum, 630 Shukert Bldg., Kansas City, Mo., Secretary.

Kentucky State Medical Association, Owensboro, Oct. 6-9. Dr. Bruce Underwood, 620 S. Third St., Louisville 2, Secretary.

Michigan State Medical Society, Grand Rapids, Pantlind Hotel and Civic Auditorium, Sept. 21-23. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing 8, Secretary.

Mississippi Valley Medical Society, St. Louis, Jefferson Hotel, Sept. 28-30. Dr. Harold Swanberg, 209-224 W. C. U. Bldg., Quincy, Ill., Secretary.

Neurosurgical Society of America, Quebec, Canada, Chateau Frontenac, Oct. 17-19. Dr. Edward Schlesinger, 710 W. 168th St., New York, Secretary.

Nevada State Medical Association, Elko, Sept. 29-Oct. 1. Dr. Roland W. Stahr, 118 California Ave., Reno, Secretary.

Oklahoma City Clinical Society, Oklahoma City, Biltmore Hotel, Oct. 24-27. Dr. F. Maxey Cooper, 512 Medical Arts Bldg., Oklahoma City, Director of Clinics.

Oregon State Medical Society, Eugene, Oct. 12-15. Dr. Werner E. Zeller, Medical-Dental Bldg., Portland 5, Secretary.

Pacific Association of Railway Surgeons, Sun Valley, Idaho, Challenger Inn, Sept. 23-25. Dr. W. T. Cummins, 1400 Fell St., San Francisco, Secretary.

Pennsylvania, Medical Society of the State of, Pittsburgh, Hotel William Penn, Sept. 26-29. Dr. W. F. Donaldson, 8104 Jenkins Arcade, Pittsburgh 22, Secretary.

Southwestern Medical Association, Albuquerque, New Mexico, Nov. 9-12. Dr. Wickliffe R. Curtis, First National Bank Bldg., El Paso, Texas, Secretary.

Southwestern Surgical Congress, Houston, Tex., Shamrock Hotel, Sept. 26-28. Dr. C. R. Rountree, 1200 N. Walker St., Oklahoma City, Secretary.

Virginia, Medical Society of, Fort Monroe, Old Point Comfort, Oct. 9-12. Miss Agnes V. Edwards, 1200 E. Clay St., Richmond, Secretary.

Western Orthopedic Association, Santa Barbara, Calif., Biltmore Hotel, Oct. 19-21. Dr. Charles W. Gilfillan, 1680 N. Vine St., Hollywood, Calif., Secretary.

Wisconsin, State Medical Society of, Milwaukee, Hotel Schroeder and Milwaukee Auditorium, Oct. 3-5. Mr. Charles H. Crownhart, 704 E. Gorham St., Madison, Secretary.

World Medical Association, General Assembly, London, Eng., Oct. 10-15. Dr. Louis H. Bauer, 2 E. 103d St., New York City, Secretary General.

GOVERNMENT SERVICES

NAVY

CORRESPONDENCE COURSES

The following correspondence courses are now available for distribution and may be obtained from the Bureau of Medicine and Surgery by qualified personnel on request.

Title of Course	Promotion Units	Retirement Points
Clinical Laboratory Procedures	3	36
Special Clinical Services—General	3	32
Tropical Medicine in the Field	2½	32
Combat and Field Medicine Practice	2½	32

All officers of the Medical Corps, Dental Corps, Medical Service Corps, Nurse Corps and Hospital Corps of the Regular Navy and Naval Reserve are eligible to enroll in any one of these courses. Enlisted personnel of the Hospital Corps are eligible to enroll in the course entitled, "Clinical Laboratory Procedures" and "Special Clinical Services—General."

Application for enrollment should be made to the Bureau of Medicine and Surgery via appropriate official channels and may be made either on NavPers-992 (application for enrollment in officer's correspondence courses) or by letter.

INDUSTRIAL MEDICINE

Under the auspices of the commandant, Third Naval District, a one week training course in industrial medicine for reserve medical officers is being offered at the School of Public Health, Columbia University, 600 W. 168th Street, New York City, Sept. 19-24.

Lecturers will be civilian military specialists in the field of industrial medicine. Comdr. L. J. Goldwater (USNR), professor of industrial hygiene, School of Public Health, Columbia University, and Lieut. Comdr. H. Tebrock (USNR) are in charge of this program. A field trip will be included to the Industrial Hygiene Laboratory, at the U. S. Naval Shipyard, Brooklyn.

Six points toward the nondisability retirement plan (Public Law 810) will be credited to each student. Naval Reserve Medical Corps officers may request one week's training duty with pay and allowances, including travel.

NEW REGULAR OFFICERS

Three reserve medical officers on active duty have been appointed to the regular Navy Medical Corps. They are:

Lieut. (jg) Lynn E. Anthony, to Navy Medical Research Unit 4, Naval Training Center, Great Lakes, Ill.

Lieut. (jg) William G. Krech (MC, USN), in a residency in surgery at the Naval Hospital, Chelsea, Mass.

Lieut. (jg) Harold M. Peacock (MC, USN), at the Attack Carrier Air Group 15.

CERTIFIED BY SPECIALTY BOARDS

Capt. M. J. Aston (MC), medical officer in command, Naval Medical School, National Naval Medical Center, Bethesda, Md., and Capt. Otto L. Burton (MC), Executive Office, Naval Hospital, Quantico, Va., have been certified by the American Board of Preventive Medicine and Public Health in the Founders Group. Capt. B. N. Ahl (MC), on duty at the Naval Hospital, Portsmouth, Va., was certified by the American Board of Ophthalmology.

PUBLIC HEALTH SERVICE

WATER POLLUTION CONTROL ADVISORY BOARD

The second meeting of the recently organized Water Pollution Control Advisory Board will be held October 3-4 in Washington, D. C. The board, appointed by the President on February 11, held its organization meeting in May and transmitted its first report to the Surgeon General of the Public Health Service on June 27. Funds were provided recently for carrying out some of the far reaching objectives of the Water Pollution Control Act. The proposed program will be reviewed at the forthcoming meeting, and plans will be made for future meetings in different parts of the country in order to obtain first hand information on water pollution problems. The new board, which brings industry, government and related interests together formally on the federal level for the first time to deal with water pollution problems, is composed of eleven members, of whom six are nongovernment leaders in pollution abatement.

GRANTS FOR RESEARCH PROJECTS

Grants totaling $489,584 to continue the financing of 35 research projects on mental and nervous disorders and grants totaling $2,554,556.00 made for training personnel in psychiatry, neurology, clinical psychology, psychiatric nursing and psychiatric social work have been announced. All grants were on recommendation of the National Advisory Mental Health Council.

Grants to training centers include funds for expanding faculty and teaching facilities and also stipends for 456 graduate students recommended by the schools. These stipends range from $1,200 to $3,600 and will be granted to 115 physicians for advanced training in psychiatry, 150 registered nurses for training in psychiatric nursing, 109 students of schools of social work for special study in psychiatric social work and 82 psychologists for training in clinical psychology.

FURTHER INCREASE IN LIFE EXPECTANCY

Figures compiled by the National Office of Vital Statistics based on the 1947 death rates show a higher life expectancy than in 1946. The average life expectancy for the total population of the United States in 1947 was 66.8 years. White women on the average live longer than any other single group, their average life expectancy at birth being 70.6 years, while the average for men is 65.2. These figures show that the average length of life of the people in the United States is nearly two years above the level reached in the three years just before the war. The expectation of life at birth has steadily increased through the last fifty years largely through control of infectious diseases.

SYMPOSIUM ON BRUCELLOSIS

A symposium on brucellosis will be held Sept. 22-23, 1949, at the National Institutes of Health, Bethesda, Md. All sessions will be in Wilson Hall, Administration Building. The veterinary, public health, clinical, bacteriologic and control aspects of the disease will be discussed. The symposium is sponsored by the Bureau of Animal Industry, the National Research Council and the National Institutes of Health.

PERSONAL

Dr. Eugene W. Green has been assigned as clinical director of the Galveston Hospital to succeed Dr. Robert T. Hewitt, who was transferred to the directorship of the Phoenix (Ariz.) Mental Health Center.

Dr. G. Robert Coatney has been appointed an adviser to the Expert Committee on Malaria of the World Health Organization by Dr. Brock Chisholm, director general of the World Health Organization.

PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Alabama

Folsom, James C.....Wilmer
Howe, Eugene H.....Tuskegee
James, Charles L.....Mobile
Lane, Robert E.....Birmingham
McRee, Jean D.....Hartselle
Morgan, James M. Jr.....Thomasville
Penton, Robert S. B.....Wetumpka
Rice, John B. McF. Jr.....Birmingham
Shugerman, Alwyn A.....Birmingham
Warren, Palmer H.....Jackson
Wright, Thomas W.....Guntersville

Arkansas

Henderson Charles T.....Hamburg
Johnston, Thomas G.....Nashville
Murphy, Horace R.....Little Rock
Ratcliff, Charles E., III.....Little Rock

Indiana

Dassel, P. M.....Hammond
Datzman, R. C.....Otterbein
Forbes, Robert J.....Martinsville
Girod, A. H.....Decatur
Griffith, R. S.....Greenfield
Hoffman, R. V. Jr.....South Bend
Lancet, R. O.....Terre Haute
Land, R. N.....Richmond
Lasser, Leonard M.....Gary
Lingeman, R. E.....Indianapolis
McIntosh, Wilbert.....Cory
Paul, Eudell G.....Whiting
Riordan, John F.....Whiting
Schlegel, Donald Max.....Brazil
Schroeder, Henry R. Jr.....Washington
Shafer, R. H.....Alexandria
Spencer, B. A.....Muncie
Stacy, George.....Whiting Lake
Stout, F. E.....Muncie
Swihart, H. R.....Elkhart
Tharp, H. R.....Franfalgan
Tilka, E. C.....E. Chicago

California

Anderson, Donald W.....Los Angeles
Ashton, Paul L.....San Francisco
Bedwell, William L.....Los Angeles
Brown, Wendell E.....San Diego
Brugge, Eugene H.....Oakland
Derry, George H.....Wilmington
Fisher, Robert B.....Los Angeles
Friend, William K.....Santa Ana
Jordan, Ernest W.....Pomona
Lieberman, Daniel.....San Francisco
McCaskill, Daniel.....San Francisco
Rea, Edward L.....Stockton

Colorado

Gladman, Richard J.....Denver
Kelsall, Charles H.....Boulder
Lapan, Joseph.....Pueblo
Mabray, Don D.....Sterling

Connecticut

Grody, Marvin H.....Hartford
Hubbard, Richmond C.....Greenwich
Kantor, Thomas G.....Westport
Mack, Daniel E.....Windsor
Shea, Joseph P. Jr.....Milford
Tamoney, Harry J.....Hartford
Yudkin, Gerald S.....Woodbridge

Delaware

Annand, John Walter.....Wilmington

District of Columbia

Janis, Leo B.....Washington
Loggins, James E. Jr.....Washington

Florida

Adams, Daniel M.....Panama City
Burns, Edward C. Jr.....Lake Wales
Hardin, Henry C. Jr.....Plant City
Kafka, Richard M.....Tampa

Georgia

Bedingfield, W. R. Jr.....Augusta
Denham, Samuel W. Jr.....Atlanta
Fisher, William R.....Macon
Fortney, Austin P.....Hapeville
Fountain, Thomas G.....Butler
Freeman, James C.....Sylvania
Gregory, Hugh H.....Dalton
Huie, Ralph A. Jr.....Atlanta
Kirkley, William H.....Fitzgerald
McElreath, Farris T. Jr.....Wadley
Reynolds, Roger J.....Atlanta
Shinall, Robert P. Jr.....Decatur
Watson, Richard P. Jr.....Savannah

Illinois

Dwyer, William B.....Chicago
Forman, Irving M.....Chicago
Grossman, Herbert J.....Chicago
Hediger, Edward L.....Pocahontas
Ihen, Menard C.....Golden
Johnson, Robert S.....Chicago
Lee, John M.....Oak Park
Levatin, Bernard I.....Chicago
Linden, Milton.....Chicago
McLaughlin, Dean E.....Centralia
Monahan, John W.....Chicago
Reed, Frank M.....Chicago
Rubin, Wallace.....Chicago
Schmutzler, Walter A.....Staunton
Seed, John C.....Oak Park
Sherman, Bennett R.....Chicago
Vruno, Michael J.....Chicago
Wilson, Lincoln E.....Tamms

Indiana

Berman, Edward J.....Indianapolis
Carberry, George A.....Gary
Donaldson, Frank C.....Lebanon
Dyke, Richard W.....Fort Allen
Kerr, Donald M.....Indianapolis
Rogers, Donald L.....New Ross

Iowa

Grams, LaVerne F.....LeClaire
Haddad, Benjamin F.....Cedar Rapids
Hennessy, Albert V.....Council Bluffs
Klein, Robert F.....Muscatine
Merritt, Floyd B.....Iowa City
Paragas, Modesto R.....Creston
Southwick, Wm. W. Jr.....Marshalltown
Van Pelt, Meredith A.....Sioux City

Kansas

Brownlee, William E.....Hutchinson
Peterson, Van D. Jr.....Overland Park
Richert, Robert C.....Newton

Kentucky

Gabbert, William R.....Greenville
Hemmer, John A.....Fort Mitchell
Kelly, James J.....Ludlow
Schell, Merrill W.....Bowling Green
Stansbury, Thomas C. Jr.....Louisville

Louisiana

Bernard, Chaille C.....Baton Rouge
Bloch, Ted.....New Orleans
Castro, Philip M. Jr.....Plaquemine
Craig, Rufus H.....Mansfield
Leckert, Edmund L. Jr.....New Orleans
Maher, Frederick A. Jr.....New Orleans
Mayer, Frank V.....New Orleans
Moskowitz, Herbert L.....New Orleans
Muhleisen, John P.....New Orleans
Sewell, Francis A.....Boyce
Taylor, John M. Jr.....Ferriday
Tucker, James W.....New Orleans
Young, Robert J.....Abbeville

Maine

Richards, Lee Warren Jr.....Augusta
Robertson, R. B.....Presque Isle
Vanamee, P.....Cape Elizabeth

Oregon

Banning, Samuel H.....Portland
Blickle, James F.....Cottage Grove
Brinton, Timmy F.....Baker
Carlin, Harry E.....Portland
Corti, George N.....Milwaukee
Earl, William H.....Cottage Grove
Ford, Floyd W.....Portland
Hansen, Vernon D.....Portland
Huestis, Gerald A.....Eugene
Keever, Joe C.....Portland
Neils, Julius K.....Portland
Standish, Vernon D.....Albany
Trainer, Joseph B.....Portland
Weinbaum, Jerome A.....Portland

Pennsylvania

Allison, James Henry.....Philadelphia
Anderson, N. S.....Philadelphia
Brackney, Edwin L.....Indiantown Gap
Chase, David Wakefield.....Erie
Davis, Ezer H.....Barnesboro
Evans, W. G. Jr.....West Pittston
Flory, R. H.....Wyncote
Gallagher, James J.....Philadelphia
Holmes, Joel G. Jr.....Philadelphia
Katz, Leon.....Pittsburgh
Lichtenfels, F. V. Jr.....Pitcairn
McCafferty, William H.....Latrobe
McLaughlin, Randall M.....Philadelphia
Pfeffer, William H.....Philadelphia
Reinsel, R. C.....Reading
Sampson, Martin C.....Philadelphia
Saylor, J. A.....Pottstown
Sherk, Carl Raymond.....Palmyra
Stockdale, Robert H.....Tarentum
Temeles, Lawrence.....Pittsburgh
Thomas, Howard P Jr.....Philadelphia
Troyen, H.....Philadelphia
Turon, L. J.....Old Forge
Van Dervort, R. S.....New Kensington

Rhode Island

Houston, Gilbert.....West Warwick
Roberts, Wesley F.....Valley Falls
Spencer, R. S.....Mansdale

South Dakota

Ensberg, Dorence L.....Toronto
Kimmel, John W.....Elk Point
Stenberg, Edwin S.....Sioux Falls

South Carolina

Allen, Harry S. Jr.....Florence
Bowie, Carroll W.....Starr
McGill, John C.....Clover
Seastrunk, Jesse G.....Columbia
Smith, Warren S.....Williams
White, Edward O.....Ehrhardt

Tennessee

Bales, Donald W.....Morristown
Daffin, Sidney E.....Memphis
Davis, James W.....Chattanooga
Douglass, Roy A. Jr.....Huntingdon
George, Charles F.....Morristown
Schack, Jerome A.....Chattanooga
Thomas, Allen G.....Davidson
Zerfoss, Thomas B. Jr.....Nashville

Texas

Blaine, Mose H. Jr.....Dallas
Boulden, Cecil F. Jr.....Austin
Couch, Ray E.....Grandview
Dick, Delfred L.....McAllen
Eidson, Jack L.....Waco
Gaitz, Charles M.....Houston
Higginbotham, Warren H.....Houston
Norman, Waymon B.....Dallas
Partain, Jack M.....San Antonio
Rittiman, Melrose C.....Orange
Tewell, Howard E. Jr.....Edinburg
Webb, Jack L.....Farmersville

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CONNECTICUT

State Society Moves to New Home.—On August 25 the offices of the Connecticut State Medical Society were moved to the society's new building at 160 St. Ronan Street in New Haven. The new home was made possible by contributions from the society's members and memorial gifts by friends of physicians. The building is a two story, L-shaped brick structure, measuring 66 by 57 feet. The first floor provides a conference room, three offices, kitchen, storage and boiler rooms. The second floor has six offices, a small conference room, a stenographic department and a mailing room. There is a parking lot in the rear of the building. Space is available in the new building for the *Connecticut State Medical Journal* offices, which for many years have been located in Hartford. It is anticipated these will soon be moved to New Haven. The society's building committee was headed by Dr. James D. Gold, Bridgeport.

ILLINOIS

Veterinarians and Health Officers Meeting.—Veterinarians and public health officers of Illinois will meet in joint session at the Abraham Lincoln Hotel, Springfield, November 16-17. Prevention and elimination of diseases of mutual danger to animals and human beings will be discussed.

State Care for Premature Infants.—From 1943 to 1948 a total of 2,532 babies received care in the State of Illinois Department of Health's three centers for the care of premature babies, and of this number 1,977, or 78 per cent, survived. The state department of health in 1943 was instrumental in establishing two centers in downstate Illinois: one at St. John's Hospital, Springfield, and one in St. Francis' Hospital, Peoria. In 1947 the third premature center was opened at Christian Welfare Hospital, East St. Louis; the fourth center began operation at St. Mary's Hospital, Quincy, in December 1948, but it is now temporarily closed for lack of personnel. These centers, when not filled to capacity, will take babies born anywhere in the state. Transportation in incubator ambulances is provided with a nurse in attendance. The state pays hospital expenses if the parents are unable to afford such special care. In 1948 public health nurses made 1,533 visits to mothers of premature infants.

Chicago

The Mayo Lecture.—The Charles H. Mayo Lecture in Surgery will be given October 21 at 2 p. m. in the Archibald Church Library of Northwestern University Medical School by Sir James Learmonth, Edinburgh, Scotland, on "Arteriovenous Communications."

Dr. Hoffman to Direct Mental Hygiene Division.—Dr. Harry R. Hoffman, formerly executive officer of the Illinois Neuropsychiatric Institute for eight years, has been named director of the Chicago Health Department's new Mental Hygiene Division. Establishment of a mental health section was recommended in the recent Chicago-Cook County Health Survey. Dr. Hoffman is on the consulting staff at Norwegian American and Norwegian Deaconness hospitals, chairman of the Illinois Psychiatric Research Council and former director of the Cook County Criminal Court behavior clinic.

Professor Taliaferro Honored.—William H. Taliaferro, Ph.D., chairman, department of bacteriology and parasitology, University of Chicago, has been elected an honorary fellow of the Royal Society of Tropical Medicine and Hygiene of London. During World War II he served on committees related to military medicine, malaria and biologic warfare of the National Research Council and was a civilian investigator on the Committee on Medical Research of the Office of Scientific Research and Development and a consultant to the surgeon general of the U. S. Army on tropical medicine research.

Personals.—Dr. Eugene J. Chesrow, professor of surgery at the Chicago Medical School, has been appointed exchange professor of surgery to the University of Haiti for 1950-1951. The government of the island recently awarded him its Legion of Honor in recognition of his work among the poor in Haiti.——Dr. John F. Pick of the University of Illinois College of Medicine returned recently from Europe where he delivered lectures at the University of Paris and in Prague.——Dr. Paul H. Jordan, assistant professor of psychiatry at the Chicago Medical School and chief neuropsychiatrist at the Veterans Administration Hygiene Clinic, has been appointed director of the State Child Guidance Clinic at Flint, Mich., effective September 1.——Dr. Leon Unger has returned from a trip to Great Britain and Ireland. He addressed the British Medical Association at Harrogate on "Nasal Allergy," the British Association of Allergists at Cardiff, Wales, and the Institute of Microbiology in London on "Bronchial Asthma" and the Association of Hospitals in Oxford on "Migraine."

Medical Society Postgraduate Courses.—The Chicago Medical Society will present a course in cardiorenal and peripheral vascular diseases October 17-22 and one in obstetrics, endocrine-gynecology and sterility October 24-29. All sessions will be held in Thorne Hall, Lake Shore Drive and Superior Street, except one evening session. The last period of each morning and afternoon session will be devoted to round table discussions. Visiting teachers include:

Benjamin M. Baker, Baltimore, Clinical Features of Coronary Artery Disease.
Irving S. Wright, New York, Use and Abuse of Anticoagulants.
George R. Meneely, Nashville, Tenn., Congestive Heart Failure.
Ovid O. Meyer, Madison, Wis., Treatment of Subacute Bacterial Endocarditis.
Alfred Blalock, Baltimore, Surgical Treatment of Congenital Heart Disease.
Robert E. Gross, Boston, Obstruction of the Esophagus or Trachea from Cardiovascular Abnormalities in the Thorax.
Francis D. Murphy, Milwaukee, Hypertensive Diseases with Special Reference to Malignant Hypertension.
John P. Merrill, Boston, Physiologic Basis of Common Diagnostic Aids in Renal Diseases.
Harris B. Shumacker Jr., Indianapolis, Aneurysms and Arteriovenous Fistulas of the Peripheral Vessels.
Franklin F. Snyder, Boston, Choice of Drugs for Analgesia in Labor.
Frank E. Whitacre, Memphis, Tenn., Diagnosis and Treatment of Bleeding in the First Trimester of Pregnancy.
John W. Harris, Madison, Wis., Postpartum Hemorrhage, Prevention and Treatment.
Ralph E. Campbell, Madison, Wis., Contracted Pelvis and Some Aspects of X-Ray Pelvimetry.
J. Robert Willson, Philadelphia, Pregnancy in the Patient with Chronic Hypertension.
Warren O. Nelson, Ph.D., Iowa City, Embryologic Relations in Malignancy.
Frank E. Adair, New York, Hormone Therapy on Metastatic Bone Disease in Cases of Breast Cancer.
Earl T. Engle, Ph.D., New York, Physiology of Menstruation.
Edwin C. Hamblen, Durham, N. C., Dysmenorrhea, Menstrual Edema and Other Cyclic Conditions.
Fred A. Simmons, Boston, Treatment of Female Infertility.
Robert S. Hotchkiss, New York, Types of Hypogonadism in the Male and Their Treatment.
Henry H. Turner, Oklahoma City, Precocious Puberty and Masculinizing Tumors of the Adrenal.

The registration for each course is limited to 100, and the fee is $50.

INDIANA

Centennial Meeting of State Association.—The Indiana State Medical Association will hold its centennial annual session September 26-29 at the Murat Temple, Indianapolis, under the presidency of Dr. Augustus P. Hauss, New Albany. Out of state speakers include:

Edward G. Billings, Denver, General Principles of Psychotherapy in General Practice.
Rolland J. Whitacre, East Cleveland, Prevention Preferred in the Operating Room.
Byrl R. Kirkland, Rochester, Minn., Bezoars of the Gastrointestinal Tract.
William T. Green, Boston, Treatment of Poliomyelitis.
Leonard A. Scheele, Washington, D. C., Physician's Role in the Fight against Cancer.
Frank C. Mann, Rochester, Minn., Hepatic Components in Some Physiologic Processes.
Udo J. Wile, Ann Arbor, Mich., Evaluation of Syphilis Therapy.
William L. Benedict, Minneapolis, Ocular Vascular Accidents.
Louis G. Herrmann, Cincinnati, Surgery of Large Arteries.
Arlie R. Barnes, Rochester, Minn., Effect of a Hormone of the Adrenal Cortex (Compound E) and of Pituitary Adrenocorticotropic Hormone on Rheumatic Fever and Rheumatic Carditis.
Max D. Garber, Rochester, N. Y., Antibiotics in Treatment of Diseases of Children.
Samuel R. Snodgrass, Galveston, Texas, Early Diagnosis of Intracranial Tumor.
Donald A. Covalt, New York, Dynamic Therapy in Chronic Disease.
Howard C. Coggeshall, Dallas, Texas, Treatment of Arthritis.

A panel on "Peripheral Vascular Diseases," with Dr. Barnes as moderator, will take place Wednesday afternoon with Drs. Benedict, Herrmann, Charles A. Hufnagel, Boston, and Harris B. Shumacker, Indianapolis, taking part. A clinicopathologic conference is scheduled for Thursday morning and a panel discussion on "Hospital Rules and Regulations" and a symposium on "Modern Management of Thyroid Diseases" Thursday afternoon. At the dinner Thursday evening Mr. Kenneth McFarland, Topeka, Kan., will speak. Section meetings, special society meetings and luncheons are included in the program. The Woman's Auxiliary to the association will meet in conjunction with the association.

MARYLAND

Meeting of General Practitioners.—The first assembly of the Maryland Academy of General Practice will be held at the Alexander Hotel, Hagerstown, September 29. The program follows:

C. Rollins Hanlon, Baltimore, Surgical Aspects of Congenital Heart Disease.
Louis A. M. Krause, Baltimore, Psychosomatic Medicine.
George M. Lyon, Washington, D. C., Radioactive Isotopes in Clinical Medicine.
Thomas H. McGavack, New York, Diseases of the Thyroid.
John B. Montgomery, Philadelphia, Office Gynecology.
Edward S. O'Keefe, Lynn, Mass., High Caloric Diet in Treatment of Diarrhea in Infancy.
Francis F. Schwentker, Baltimore, Rheumatic Fever.
LeRoy H. Sloan, Chicago, Changing Patterns of Disease.

The registration fee is $5.

MASSACHUSETTS

Dr. Moritz Goes to Western Reserve.—Dr. Alan R. Moritz, head of the department of legal medicine at the Harvard Medical School, Boston, left September 3 to take up his new duties as professor of pathology and director of the Institute of Pathology at Western Reserve University, Cleveland. Before his departure the Massachusetts Medico-Legal Society at a special meeting presented to Dr. Moritz a scroll in recognition of his services. In his honor the society installed at the Harvard Medical School a bronze plaque commemorating his ten years of service which have "given legal medicine a new integrity and stature in the Commonwealth of Massachusetts," and it presented a sum of money to the school. Dr. Moritz has been a leader in the movement for the application of medical knowledge to the detection of crime and the investigation of deaths of unknown origin. In a series of seminars at Harvard he has trained many police officers, medical examiners and coroners from eastern states and the Middlewest. He is chairman of the Committee of the American Medical Association to Study the Relationships of Medicine and Law. He also lectured on legal medicine at the medical schools of Boston University and Tufts College. In addition to serving since 1939 as pathologist to the Massachusetts Department of Public Welfare, he was associate medical examiner of Suffolk County, pathologist in chief at Peter Bent Brigham Hospital and consultant at Children's Hospital. Dr. Moritz was graduated from the University of Nebraska College of Medicine in 1923. His postgraduate training in pathology was taken at Western Reserve University, the Lakeside Hospital of Cleveland and at the City Hospital of Vienna, Austria. He taught at Western Reserve and served as pathologist in charge, University Hospitals, Cleveland, before joining the Harvard faculty in 1937.

MISSOURI

Study Club Program.—The following programs for the remainder of 1949 have been arranged by the General Practitioners Study Club, St. Louis, to be held in Lecture Hall:

September 21, 9 p. m., Roy V. Boedeker, St. Louis, Management of Chronic Cervicitis; film on cervicitis.
October 19, 8 p. m., Phonographically Reproduced Heart Sounds of Valvular Lesions, and film, Management of the Failing Heart; James B. Stubbs, St. Louis, Changing Concepts of Congestive Heart Failure; Victor A. Bell, New York, Why the Recent Adverse Criticism of Digitoxin?
November 16, 9 p. m., Gilbert B. Forbes, St. Louis, Management of Convulsive Disorders and film on Allergy: Immunology and Treatment.
December 21, 9 p. m., Dr. Adolph H. Conrad Jr., St. Louis, Differential Diagnosis and Treatment of Common Skin Diseases; film on Hypothyroidism: Diagnosis, Etiology, Treatment.

NEW MEXICO

Medical Conference and Cancer Society Meeting.—The Southwestern Medical Conference and New Mexico Division of the American Cancer Society will meet at the Hilton Hotel, Albuquerque, November 9-12. Speakers include:

Evans W. Pernokis, Chicago, Anemias and Leukemia.
Elmer Belt, Los Angeles, Ureteral Intestinal Anastomosis.
Herbert W. Meyer, New York, Cancer of the Breast.
Donald M. Pillsbury, Philadelphia, Malignant Skin Lesions.
Allan M. Butler, Boston, Malignancies in Childhood.
Herbert F. Traut, San Francisco, Use of Vaginal Smear in General Gynecologic Diagnosis.
Otto C. Brantigan, Baltimore, Surgical Treatment of Peptic Ulcers.
William A. Rettberg, Denver, Present Status of Antibiotics.
William Boyd, Toronto, Ontario, Canada, subject to be announced.
Kenneth D. A. Allen, Denver, subject to be announced.

For reservations and information address Dr. Alvin H. Follingstad, care of the Chamber of Commerce, Albuquerque, N. Mex.

NEW YORK

Society News.—The Medical Society of the State of New York in cooperation with the New York State Department of Health has arranged a postgraduate lecture for the Jefferson County Medical Society meeting September 20 at 8 p. m. at the Black River Valley Club, Watertown. Dr. Robert F. Korns, Albany, will speak on "Epidemiology of Poliomyelitis."——The Utica Academy of Medicine meeting October 20 at 8 p. m. at the Hotel Utica will hear Dr. George A. Perera, New York City, speak on "Action and Use of the Adrenal Cortical Steroids, Including Cortisone."——The Geneva Academy of Medicine will hear Dr. Joe W. Howland, Rochester, speak on "Current Developments in the Use of Radioactive Materials for Medical Purposes" at a meeting September 19 at 8:30 p. m. in the Bellhurst Restaurant, Geneva.

Richard H. Hutchings Memorial Award.—A memorial lecture in honor of the late Dr. Richard H. Hutchings, former editor of *The Psychiatric Quarterly*, will be given at Syracuse University October 3, 8:30 p. m., in the auditorium of the College of Medicine. The lecturer will be Dr. Winfred Overholser, superintendent of St. Elizabeths Hospital, Washington, D. C., and his subject "Modern Trends in Psychiatric Treatment." A special memorial award of $100 to be presented by the committee for an outstanding contribution to psychiatry from a public mental institution has also been announced by Dr. Harry A. Steckel, chairman of the permanent memorial committee. It is presented by an anonymous donor through Dr. C. Charles Burlingame, psychiatrist in chief at the Institute of Living, Hartford, Conn., a member of the permanent memorial committee. Scientific articles, reports or nominations for the award may be submitted to Dr. Steckel or to Dr. Newton Biegelow, secretary-treasurer of the committee. Dr. Hutchings was superintendent of St. Lawrence Hospital, New York, and of Utica State Hospital, Utica, for many years. The memorial fund is still open for contributions. The fund, now totalling about $1,500, will be used solely for lectureship honoraria. All future contributions will be used for lectureship purposes unless otherwise specified by the donor.

New York City

Dr. Rusk Makes European Trip.—In his capacity as consultant in rehabilitation to the department of social affairs of the United Nations, Dr. Howard A. Rusk, chairman, department of rehabilitation and physical medicine, New York University College of Medicine, left for Europe early in September to participate in teaching seminars on rehabilitation. He will confer with officials of the World Health Organization in Geneva, Switzerland, of UNESCO in Paris, observe rehabilitation activities in England and return to New York in late October.

Personals.—Dr. Isidore H. Goldberger has been appointed director of health education of the Board of Education of the City of New York.——Dr. Rustin McIntosh has been elected president of the medical board of the Presbyterian Hospital; Dr. Howard C. Taylor Jr. succeeds him as vice president. Dr. George F. Cahill, former president, will retire after three years as president of the board. Dr. McIntosh is also Carpentier Professor of Pediatrics, Columbia University College of Physicians and Surgeons. Dr. Taylor is professor and chairman of the department of obstetrics and gynecology at the college.——Dr. Claude W. Munger, former director of St. Luke's Hospital, has received the 1949 award of merit of the American Hospital Association. He was cited for having advanced education and standards of hospital administration and for his leadership in health organizations. Dr. Munger retired last year as director of St. Luke's because of ill health.——Dr. Robert Ward, associate professor of pediatrics at the New York University College of Medicine has been appointed full professor of pediatrics.

PENNSYLVANIA

Benjamin Rush Awards.—The Emergency Aid of Pennsylvania, with headquarters in Philadelphia, and Mrs. Leonard D. Doggett of State College will receive the Benjamin Rush Awards for 1949, annual presentations made by the state medical society to the lay individual and the lay organization making the outstanding contributions to the health of the people of the commonwealth. Bronze medallions bearing a likeness of Dr. Benjamin Rush, a native Pennsylvanian, will be presented at the ninety-ninth annual session of the medical society in Pittsburgh September 27. Long a leader in health activities in Centre County, Mrs. Doggett has been active with the local Red Cross unit, the local cancer society, State College Nurses Association and Centre County Hospital (Bellefonte) Auxiliary and is chairman of the Health Com-

mittee of the Business and Professional Women's Club of State College. She was the first woman on the Centre County Hospital Board and has promoted and aided local legislation for better sanitary conditions in restaurants and for better water and sewage disposal facilities. Mrs. Doggett was nominated for this honor by the Centre County Medical Society.

Emergency Aid of Pennsylvania is a voluntary organization of women established in 1914, the objective of which is emergency relief work for the benefit of the military forces and civilian population of the United States and its allies. The organization is supported by dues from its 1,984 members and by proceeds from various projects and is registered and approved by the state department of welfare. Emergency Aid has provided transportation service for cerebral palsy patients to and from clinics, distributed gifts annually to all tuberculous patients in Municipal and Philadelphia General hospitals, Philadelphia, mended hospital garments, sponsored after-school recreation in public schools and in recent months has provided clothing, shoes, medical supplies and other aid to 2,301 families.

SOUTH DAKOTA

State Medical Election.—The South Dakota State Medical Association at its annual meeting installed Dr. William H. Saxton, Huron, as president and chose Dr. Clarence E. Robbins, Pierre, president-elect. Dr. Roland G. Mayer, Aberdeen, was elected secretary-treasurer.

TEXAS

Fund to Establish Instructorship.—Baylor University College of Medicine, Houston, has recently received a gift of approximately $53,000 to establish an instructorship. A cash donation of $3,000 and undivided oil royalties valued at $50,000 were made available by Mr. and Mrs. B. M. Goldsmith of Quitman as a memorial to their father, the late Dr. John B. Goldsmith. The fund will be administered by the Texas Baptist Foundation.

Southwestern Medical College to Become State University.—On request of the Board of Regents of the University of Texas, the house of delegates of the State Medical Association of Texas at their meeting July 13 selected Dallas as the site of a new medical branch of the university, and the regents accepted the offer of the Southwestern Medical Foundation to take over facilities of Southwestern Medical College. On September 1 the foundation turned over $1,408,000 in properties, buildings, library and equipment to the University of Texas. Plans are being made to increase the enrolment of the school for the fall term. The new medical branch was authorized during the recent session of the state legislature, which had instructed the house of delegates of the State Medical Association of Texas to survey and make a choice of location of the establishment of the medical school. Dallas, San Antonio and Temple were surveyed, and El Paso submitted information. The new branch will be known as Southwestern Medical School. The Southwestern Medical Foundation, which has operated the college for six years, is losing control to the state, but the school will remain the primary concern of the 11 year old foundation. According to Dr. Eben H. Cary, foundation president, its $2,000,000 in assets will be retained to help on faculty salaries and research. It is expected that other buildings will be erected for the medical school on a 40 acre site for a proposed medical center. In addition to drawing its premedical students from the University of Texas, it will serve as a medical school for Southern Methodist University, Texas Christian University, North Texas State College, Texas State College for Women and Arlington State College, all of which are within commuting distance.

WASHINGTON

Course in Surgery.—The Washington State Medical Association has arranged a graduate course in surgery September 26-30 at the King County Hospital in Seattle. The programs will begin at 9 a. m. and close at 4 p. m. The program chairman is Dr. John K. Martin.

Cerebral Palsy Center.—A new center for the medical and educational care of cerebral palsied children in Seattle was opened September 1 at Firland Sanatorium replacing the center located at McKay Memorial Research Hospital, Soap Lake. It is being operated jointly by the departments of public instruction and health under a special legislative appropriation. About 20 children were expected to be in residence by September 1. A professional advisory committee will be set up, consisting of representatives of schools, and a lay advisory committee will advise on matters of policy.

WISCONSIN

Cancer Teaching Clinic.—The Interurban Academy of Medicine will present a Cancer Teaching Clinic at the Hotel Superior, Superior, September 21 under the sponsorship of the 11th Councilor District, St. Louis County Medical Society and the Wisconsin Division of the American Cancer Society. There will be no registration fee. The program, which is financed through funds of the Wisconsin Division, American Cancer Society, and which will begin at 2 p. m., includes:

Gordon B. New, Rochester, Minn., Oral Cancer.
Motion picture: Cancer—The Problem of Early Diagnosis.
Walter G. Maddock, Chicago, Carcinoma of the Biliary Tract.

A symposium and question and answer period will follow the presentations. At the dinner session Dr. Robert A. Huseby, Minneapolis, will speak on "Recent Advances in Cancer, Their Evaluation and the Future Outlook of Treatment."

State Medical Meeting.—The State Medical Society of Wisconsin will hold its annual meeting at the Milwaukee Auditorium, Milwaukee October 1-5. Visiting speakers include:

Richard B. Capps, Chicago, Treatment of Liver Disease.
Robert L. Ward, New York, Diagnosis and Treatment of Poliomyelitis in the Early Stage.
Joe R. Brown, Minneapolis, Correlation of the Pathology, Symptomatology and Treatment of Bulbar Poliomyelitis.
Arthur C. Curtis, Ann Arbor, Mich., Sarcoid Disease.
Jessie C. Gray, Toronto, Canada, Carcinoma of the Rectum.
Reynold A. Jensen, Minneapolis, The Physician and Mental Health.
Winthrop M. Phelps, Baltimore, The Cerebral Palsied Child.
Heyworth N. Sanford, Chicago, Problems in Care of the Newborn.
Ivan B. Taylor, Detroit, Anesthesia, the Weakest Link in Surgical Procedure.
Nelson W. Barker, Minneapolis, Diagnosis and Treatment of Chronic Occlusive Arterial Disease of the Extremities.
Frederick Coller, Ann Arbor, Mich., Diagnosis and Management of Lesions of the Breast.
James W. J. Carpender, Chicago, Irradiation Therapy with Particular Attention to Radioactive Isotopes.
Lester R. Dragstedt, Chicago, Physiologic Principles in Surgery of the Stomach.

Dr. Ralph J. Gampell, San Francisco, lately of the University of Manchester, England, will speak at the annual dinner Tuesday on "Socialized Medicine as I Saw It." Clinical conferences will be held Monday at the Milwaukee Auditorium by staffs of Milwaukee hospitals. Round table luncheons with a limited attendance and motion picture programs are scheduled for each day. Section meetings will be held in internal medicine, obstetrics and gynecology, ophthalmology and otolaryngology, pediatrics, radiology and surgery. The Woman's Auxiliary will meet October 2-4 at the Hotel Schroeder.

WYOMING

Orthopedic Conferences.—The Wyoming State Department of Public Health will conduct orthopedic conferences for crippled children under 21 years of age September 23 through October 8. Physicians should refer new patients to the state department of public health before the conference, so that approximate attendance can be anticipated. Former patients should not attend unless invited. New patients are requested to furnish record of a recent general physical examination by a physician. Conferences will be held at the following places with Dr. Gordon Whiston, Casper, as orthopedist: September 23, Gillette; September 24, Worland; September 30, Cheyenne; October 1, Laramie; October 7, Kemmerer, and October 8, Rock Springs.

GENERAL

Change Pan American Conference Dates.—In order to accommodate a group of Mexican doctors who will attend the International Pediatrics Convention in Mexico City, the dates of the Second Congress of the Pan American Women's Alliance to be held in Los Angeles have been changed from November 1-6 to November 12-17.

Plague Infection in Fleas.—The U. S. Public Health Service reports that under date of July 8 plague infection was reported proved in specimens of tissue and ectoparasites from ground squirrels collected in Beaverhead County, Mont., on a ranch 24 miles northwest of Dillon on the Jackson road. Under date of July 29, plague infection was reported proved in specimens of fleas collected in Thomas County, Kansas, from two grasshopper mice and in fleas recovered July 13 by flagging abandoned burrows of prairie dogs. In Rio Arriba County, New Mexico, plague was reported proved in fleas from white-footed mice trapped July 12.

Meetings on Anesthesiology.—The Committee on Post-Graduate Education of the New England Society of Anesthesiologists has arranged a series of meetings on the management of surgical patients from the standpoint of the anesthesiologist, to be held at the Bigelow Amphitheatre, Massachusetts General

Hospital, 2 to 5 p. m., the first Saturday of each month, October through February 1950. All interested physicians are invited to attend.

Oct. 1, Circulatory Management of Surgical Patients.
Nov. 5, Respiratory Management of Surgical and Obstetrical Patients.
Dec. 3, Damage to the Nervous System Incident to Surgery and Anesthesia.
Jan. 7, Management of Analgesia and Anesthesia for Obstetrics.
Feb. 4, Management of Anesthesia for Children.

Further information may be obtained from Dr. Julia G. Arrowood, Massachusetts Memorial Hospitals, 750 Harrison Avenue, Boston 18.

Prevalence of Poliomyelitis.—Reports of cases of poliomyelitis for the periods indicated have been received from the National Office of Vital Statistics, U. S. Public Health Service.

Division and State	Week Ended Sept. 3, 1949	Week Ended Sept. 4, 1948	Median Expec.	Jan. 1 to Sept. 3, 1949	Jan. 1 to Sept. 4, 1948	Total* March 19-Sept. 3, 1949	Total* March 20-Sept. 4, 1948
New England States:							
Maine	37	4	4	261	19	261	19
New Hampshire	24	3	3	113	10	113	10
Vermont	15	1	5	57	14	55	13
Massachusetts	194	12	26	931	98	931	95
Rhode Island	17	..	1	67	...	67	...
Connecticut	50	9	13	291	62	288	61
Middle Atlantic States:							
New York	538	101	101	3,113	601	3,093	565
New Jersey	137	56	56	703	321	667	314
Pennsylvania	78	51	51	347	311	337	300
East North Central States:							
Ohio	171	65	43	892‡	539	886	530
Indiana	61	39	27	685	196	675	186
Illinois	282	87	96	1,805	445	1,789	438
Michigan	287	48	59	1,586‡	249	1,586‡	261
Wisconsin	101	39	32	516	190	502	190
West North Central States:							
Minnesota	168	90	40	1,079	457	1,040	449
Iowa	72	53	24	693‡	381	680‡	368
Missouri	101	12	12	918	118	907	118
North Dakota	52	38	11	341	65	337	65
South Dakota	38	21	4	204	93	182	93
Nebraska	39	27	13	295	305	282	300
Kansas	52	28	15	447	138	421	135
South Atlantic States:							
Delaware	4	7	4	33	97	31	96
Maryland	13	3	8	87	32	78	31
District of Columbia	7	11	8	48	60	47	60
Virginia	27	31	31	190	289†	180	287†
West Virginia	23	12	5	227	78	220	73
North Carolina	9	137	10	150	1,896	132	1,872
South Carolina	4	23	4	69	258†	56	250†
Georgia	5	13	8	114	151	106	150
Florida	14	12	4	155	176	134	159
East South Central States:							
Kentucky	60	11	6	353	119	345	116
Tennessee	36	34	18	339	216	333	209
Alabama	13	10	9	150	128	146	116
Mississippi	6	8	7	220	87	209	85
West South Central States:							
Arkansas	44	9	4	760	95	749	93
Louisiana	7	10	7	152	85	140	79
Oklahoma	50	14	14	871	234	864	228
Texas	63	52	23	1,669	1,308	1,578	1,287
Mountain States:							
Montana	8	6	2	33	34	32	24
Idaho	27	3	3	296	84	283	57
Wyoming	7	2	2	68	56	68	56
Colorado	55	13	13	328	57	326	55
New Mexico	16	4	2	108	49	107	47
Arizona	11	11	3	106	72	95	71
Utah	19	3	3	110	37	94	34
Nevada	1	1	..	11	3	11	2
Pacific States:							
Washington	50	9	12	308	117	263	99
Oregon	9	8	8	106	66	90	50
California	89	264	33	1,318	2,141	1,029	2,109
Total	3,197	1,505	.....	23,740‡	12,657†	22,824‡	12,307†
Median, 1944-1948			1,505		9,474		9,211

*Last two columns show reported incidence since approximate seasonal low: 24 weeks.
†Corrected figures.
‡ Current corrections (made in cumulative totals): Michigan, deduct 2 cases for week ended August 27; Iowa, add 32 cases for week ended August 27.

Care Book Program.—The U. S. National Commission for UNESCO and the National Research Council's Committee on UNESCO have formulated the UNESCO-Care Book Plan, under which Care will distribute "Book Packages." The program is aimed at supplying scientific and cultural institutions abroad with technical books to bring about scientific and cultural reconstruction. The book lists, which are not issued publicly by Care, are made up of textbooks for college and graduate study, most of which have been published since 1940. Care undertakes to accept gifts of money from American scientists and in return assumes the responsibility of purchasing and shipping the books to institutions abroad. Although Care hopes that the majority of contributions will be undesignated, donors of $10 or more may specify one or all of the following: country, type of institution, category or categories of books. If a donor of $10 or more desires to name a specific institution, he may do so. It will be helpful if he also specifies the category of books to be sent. Books cannot be sent to individuals. This is not a used book program and donors should not send books. Checks and money orders should be sent to Care Book Program, Care, 20 Broad Street, New York 5. This program has been developed in cooperation with UNESCO, the Library of Congress, the American Library Association, medical and scientific associations, and governmental authorities overseas. The advisory Committee on Voluntary Foreign Aid of the United States State Department has approved the project. The American Medical Association has approved a nationwide program for the medical profession, and the Board of Trustees of the Association has appointed a special committee to work out the details of the Care-A. M. A. program.

Indictment for Price Fixing on Medical X-ray Film.—Attorney General J. Howard McGrath announced September 1 that a federal grand jury at Los Angeles returned an indictment charging six corporations and four persons with violating the Sherman Antitrust Law by fixing prices on medical x-ray film sold in the Southern California areas. The following corporations and individuals were named as defendants in the indictment:

General Electric X-ray Corporation, Milwaukee.
Kelcket X-Ray Sales Company of Los Angeles, Los Angeles.
Kelley-Koett Manufacturing Company, Cincinnati.
R. L. Sherer Company, Los Angeles.
Westinghouse Electric Corporation, Pittsburgh.
Henry N. Beets, doing business as Henry N. Beets Company, 2611 W. 7th Street, Los Angeles.
Geoffrey Grayston, formerly doing business as Grayston X-Ray Company, 1814 W. 9th Street, Los Angeles.
F. Clair Morgan, doing business as F. Clair Morgan Company, 1831 W. 9th Street, Los Angeles.

The indictment charges the defendants with having entered into a conspiracy to fix the prices at which medical x-ray film was sold to hospitals, doctors, roentgenologists, x-ray laboratories, clinics and other users in the Southern California area, where approximately $4,000,000 worth of medical x-ray film is sold annually. The defendants are also charged with having rotated and fixed prices on bids submitted for the Los Angeles County Hospital business during the period 1946 to 1948. The purchases of medical x-ray film by the county hospital amount to about $100,000 per year.

Announcing the return of the indictment by the Los Angeles Federal Grand Jury, the attorney general said, "This is another in a series of cases brought by the Department of Justice to eliminate restraints of trade in a field vital to public health. Illegal conspiracies of the type here charged increase the cost of medical services to the public and increase the operating cost of public health service." The case is under the general supervision of Marcus A. Hollabaugh, chief of the Special Litigation Section of the Antitrust Division.

CORRECTION

Postgraduate Courses.—In the extensive list of postgraduate courses in THE JOURNAL of June 25, the course in basic sciences of ophthalmology offered by Tulane University School of Medicine, given annually July 1 through April 30, was inadvertently omitted.

"Maternal Deaths from Coccidioidomycosis."—Smale and Birsner in their paper on this subject in THE JOURNAL, August 6, page 1152, stated that a search of literature failed to discover a single publication concerning the occurrence of disseminated coccidioidomycosis during pregnancy. Dr. Smale now writes that they were in error and, in the preparation of their paper, had overlooked a report on this subject by Mendenhall, Black and Pottz in the *Rocky Mountain Medical Journal*, June 1948, page 472.

Marriages

JOHN E. ROCKWELL JR., San Carlos, Calif., to Miss Blanche Guerin of San Francisco, June 24.

WILLIAM J. LITTLE JR., Racine, Wis., to Miss Dorothy Kraudelt in Dearborn, Mich., June 18.

JOHN T. CRISSEY, Tonawanda, N. Y., to Miss Alice Hogue of Buffalo, in Atlanta, July 30.

Deaths

Bonnelle William Rhamy ✠ Fort Wayne, Ind.; born in Findlay, Ohio, Feb. 11, 1874; Fort Wayne College of Medicine, 1898; professor of physiology at his alma mater from 1902 to 1904; city bacteriologist in 1905; specialist certified by the American Board of Pathology; charter member of the American Society of Clinical Pathologists and for many years a member of the Indiana State Council; one of the founders of the Indiana State Pathological Association; member of the College of American Pathologists, American Association for the Advancement of Science, National Geographical Society, American Heart Association, Fort Wayne Academy of Science and the venereal disease control commission of the Indiana State Medical Association; member of the Chamber of Commerce, Institute of American Genealogy and the Virginia Historical Society; served in France and Germany during World War I; member of the Indiana Medical Advisory Board no. 4, Selective Service System; at various times pathologist at the Defiance (Ohio) Hospital, Sacred Heart Hospital, Garrett, Wells County Hospital, Bluffton, Parkview Hospital, Plymouth, Woodlawn Hospital, Rochester, Lutheran, Methodist and St. Joseph's hospitals; clinical pathologist and founder of the Fort Wayne Medical Laboratory; member of the "Fifty Year Club" of the Indiana State Medical Association; died May 26, aged 75, of arteriosclerotic heart disease and diabetes mellitus.

Staige Davis Blackford ✠ Charlottesville, Va.; born in Alexander, Va., Dec. 28, 1898; University of Virginia Department of Medicine, Charlottesville, 1925; professor of the practice of medicine and chairman of the clinical staff at his alma mater; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians and the American Clinical and Climatological Association; during World War I served with the University of Virginia section of the Army Ambulance Service and was decorated with the Croix de Guerre; during World War II chief of the medical service of the 8th Evacuation Hospital in North Africa and Italy for thirty months and was awarded the Legion of Merit for his work in that hospital; decorated with the Medal of French Morocco; recently elected editor of the University of Virginia Medical Alumni Bulletin; on the staff of the University of Virginia Hospital, where he died July 17, aged 50, of coronary thrombosis.

Max Alexander Novey, Baltimore; born in New York Sept. 23, 1899; Johns Hopkins University School of Medicine, Baltimore, 1923; assistant professor of obstetrics at the University of Maryland School of Medicine and College of Physicians and Surgeons; lecturer on public health administration, Johns Hopkins University School of Hygiene and Public Health; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; director of the department of child hygiene, city health department; a member of the board of trustees and the medical advisory board of the Maryland Rheumatic Fever Association; affiliated with Mount Sinai Hospital, South Baltimore General Hospital and Provident Hospital and Free Dispensary; died July 16, aged 49.

William Denton Rowland ✠ Boston; born in Greencastle, Pa., Dec. 6, 1879; University of Michigan Homeopathic Medical School, Ann Arbor, 1911; professor emeritus of ophthalmology at the Boston University School of Medicine; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the New England Ophthalmological Society; fellow of the American College of Surgeons; served in the medical corps of the U. S. Army during World War I; affiliated with Massachusetts Memorial Hospitals; consulting ophthalmologist, Westborough (Mass.) State Hospital and the Leonard Morse Hospital in Natick; died July 1, aged 69, of hypertensive vascular disease.

Jacob John Westra ✠ Champaign, Ill.; born in Grand Rapids, Mich., March 2, 1908; Rush Medical College, Chicago, 1937; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; secretary treasurer of the Champaign County Medical Society; member of the Champaign County Chapter of the American Cancer Society; an associate of the American College of Physicians; entered the Mayo Foundation in Rochester, Minn., as a fellow in April 1938 and remained until Oct. 1, 1939; associated with the Christie Clinic; on the staffs of Burnham City Hospital in Champaign, McKinley Hospital and Mercy Hospital in Urbana, where he died July 17, aged 41, following a cholecystectomy.

Joseph James Anderson, Richmond, Va.; Medical College of Virginia, Richmond, 1893; member of the American Medical Association; died May 19, aged 79, of pulmonary embolism.

Harold M. Brown, Klamath Falls, Ore.; John A. Creighton Medical College, Omaha, 1904; served during World War I; affiliated with Hillside and Klamath Valley hospitals; died May 16, aged 76, of cerebral hemorrhage.

Claude Lester Davis, Hinesville, Ga.; Emory University School of Medicine, Atlanta, 1916; member of the American Medical Association; served during World War I; died at his home May 21, aged 58, of coronary thrombosis.

Lyman Edwin Dockry ✠ San Diego, Calif.; Marquette University School of Medicine, Milwaukee, 1917; member of the State Medical Society of Wisconsin; past president of the Brown-Kewanee-Door Counties Medical Society in Wisconsin; served in the regular U. S. Navy during World War I and in the U. S. Naval Reserve during World War II; died in the U. S. Naval Hospital May 19, aged 56, of hypertensive heart disease.

Herman H. Kamman ✠ Columbus, Ind.; Kentucky School of Medicine, Louisville, 1903; formerly secretary and vice president of the Bartholomew County Medical Society; served as county health officer, city health officer and county coroner; on the staff of the Bartholomew County Hospital; died May 20, aged 77, of cerebral hemorrhage and arteriosclerosis.

William Sargeant Knox, West Lebanon, Pa.; University of Pittsburgh School of Medicine, 1937; served during World War II; suffocated May 24, aged 36, as a result of fire caused by a cigaret he was smoking while in bed.

Herbert Boyd Masten, Springer, N. Mex.; Columbia University College of Physicians and Surgeons, New York, 1893; affiliated with Springer Hospital; died May 19, aged 79, of coronary thrombosis.

Robert Graham Morrison, Denver; Denver and Gross College of Medicine, 1903; died May 17, aged 72, of perforated duodenal ulcer.

Harry Baron Press, Los Angeles; Drake University Medical Department, Des Moines, 1908; died in the Queen of Angels Hospital May 25, aged 62, of injuries received when struck by an automobile.

Jacob J. Roth, Newark, N. J.; Universitat Zürich Medizinische Fakultät, Switzerland, 1908; died in Passaic recently, aged 66, of cancer of the rectum with metastases.

Walter Franklin Sowers, Baltimore; University of Maryland School of Medicine, Baltimore, 1906; police surgeon for many years; served on the staff of Maryland General Hospital, where he died May 31, aged 67.

Charles Paul Stockdale, Boulder, Colo.; State University of Iowa College of Medicine, Iowa City, 1905; Barnes Medical College, St. Louis, 1908; died May 4, aged 69, of pneumonia.

Jacob Talso ✠ Ishpeming, Mich.; Chicago College of Medicine and Surgery, 1910; died in St. Luke's Hospital, Marquette, May 30, aged 76, of acute coronary occlusion.

Robert Wiley Thompson, Weslaco, Texas; Vanderbilt University School of Medicine, Nashville, 1895; University of Nashville Medical Department, 1895; formerly practiced in Lumberton, Miss., and from 1914 to 1916 a member of the Mississippi State Board of Health; died in Corpus Christi May 3, aged 80, of heart disease.

Wesley B. Wasson ✠ Nixa, Mo.; University of Louisville (Ky.) Medical Department, 1890; an Associate Fellow of the American Medical Association; past president of the Christian County Medical Society; died May 20, aged 86, of carcinoma of the intestine.

Henry C. Watkins, Memphis, Tenn.; Memphis (Tenn.) Hospital Medical College, 1901; died in the Methodist Hospital May 18, aged 77, of carcinoma of the colon.

Walter Lewis Williams, Brookneal, Va.; Medical College of Virginia, Richmond, 1885; member of the American Medical Association; charter member of the Lynchburg Academy of Medicine; died in the Virginia Baptist Hospital, Lynchburg, June 26, aged 88.

George Forest Wright ✠ Johnstown, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1921; at one time health officer of Franklin and Conemaugh boroughs; served as school physician for Conemaugh; associated with the Conemaugh Valley Memorial Hospital, Mercy Hospital and the Lee Homeopathic Hospital, where he died June 8, aged 56, of cerebral hemorrhage.

George Augustus Yaeger, Chicago; Rush Medical College, Chicago, 1885; died June 22, aged 82, of bronchopneumonia.

Foreign Letters

ITALY

(From Our Regular Correspondent)

FLORENCE, July 15, 1949.

Second World Assembly of Health

The second World Assembly of Health was held in Rome June 13-July 2 on the invitation of the Italian government. The site was the historic Venetian Palace, which had been suitably reorganized with technical and sanitary services under supervision of a secretarial office created by the high commissioner for Hygiene and Public Health, Prof. Mario Cotellessa. The plenary sessions took place in the great Sala Regia where each delegate was furnished with a small radiophonic apparatus with a cap which permitted listening to the reports in various languages with translations at the same time they were presented.

Concerning malaria, the World Health Organization supported the various governments in the campaign against this disease, and it stimulated public opinion so that suppression of this scourge may be on a worldwide scale. Only 4 deaths due to malaria were reported in 1948, which is the lowest annual incidence in Italian history. In one of the major islands belonging to Italy, Sardinia, there was complete suppression of Anopheles, through an energetic campaign carried out under the auspices of the Italian government and the Rockefeller Foundation.

The World Health Organization has maintained close contact with the Italian government, to which it has given advice and technical assistance by a committee of experts. Dichlorodiphenyltrichloroethane (DDT) was the main weapon used in the island of Sardinia in the campaign against the Anopheles.

In Greece, as the result of the antimalarial campaign, in certain regions the incidence of the disease was reduced from 85 to 5 per cent.

Four thousand and seven hundred localities in Greece were treated with DDT, and 28,500 hectares of mosquito-infested soil were dusted from the air with DDT.

Antimalarial action on a large scale has been planned under the auspices of the World Health Organization in numerous other countries.

In the fight against tuberculosis, the health services of various nations have received direct support from the World Health Organization in the form of demonstration units, instruction by expert consultants, special courses and information about the most recent technical problems and about the value of new therapeutic agents, such as streptomycin.

The World Health Organization has cooperated with the Danish Red Cross, Scandinavian organizations and the Intertional Funds of the United Nations for Children's Help, with the aim of activating a program to identify tuberculous persons by means of the tuberculin reaction and to carry out BCG vaccination on a large scale. In Europe alone 9,000,000 infants and children were examined and 3,500,000 vaccinations performed. The campaign has been extended to many countries in Asia, in the Mediterranean East, in North Africa and in Latin America. Probably about 100,000,000 persons will be benefitted by this campaign.

In the field of venereal diseases, the situation after the war presented two noteworthy facts: (1) the alarming increase in the number of affected persons—in the United States alone the loss in production caused by venereal diseases has been calculated as more than $100,000,000 for 1946—and (2) the primary importance of penicillin in the treatment of venereal diseases.

Poland, after consultation with the World Health Organization, was the first country in Europe to carry out an effective attack against venereal diseases based on treatment with penicillin. Within a few months more than 500,000 persons were examined, 75,000 of whom were cured with penicillin, the total cost of which was about $385,000.

An international committee of experts called together by the World Health Organization recommended the extension of the campaign against diphtheria, whooping cough and other diseases of children, in addition to the antisyphilitic and antimalarial campaign.

Mental Health

Of considerable importance is the work developed by the World Health Organization in the field of mental health. The problems of mental hygiene pertain in nearly all the branches of medicine and are taken into consideration by the World Health Organization in dealing with alcoholism and toxicomania and in programs for the campaign against tuberculosis, venereal diseases and malaria. An investigation of psychoneuroses has demonstrated that in an industrial unit the neuropathic disturbances caused a loss in working hours which was greater than that caused by common colds.

In Ethiopia, Greece and China, the World Health Organization has given practical assistance. Urban quarters had been dusted with DDT with the aim of destroying hematophagous insects; the water supplies have been restored, and appropriate methods for removal of refuse have been introduced. Sanitary measures have been organized for the refugees from Palestine in conjunction with aid given by the national units; thus the danger of epidemics among the 800,000 persons in the refugee camps of Lebanon, Palestine, Syria and Transjordan has been lessened.

For 1950 an extensive program of work has been traced, based on an ordinary budget of $7,893,000 and completed from an extraordinary budget of $9,152,520. The main items of this program are: the creation of a "model area" in a locality affected by endemic diseases; continuation of the antimalarial campaign; increase of maternal and infantile hygiene and campaigns with respect to mental hygiene, venereal diseases, tuberculosis, infectious diseases, virus diseases and diseases of children. In addition, the publication of an international pharmacopeia will be undertaken for the first time in history.

Surgical Treatment of Hypertrophic Prostate

At the Medical Academy of Genoa, Prof. G. Nicolich discussed surgical treatment of the hypertrophic prostate.

In four years Professor Nicolich performed 180 prostatectomies or resections of the neck of the bladder by the transvesical route with a mortality rate of 3.3 per cent, 27 perineal prostatectomies with a higher mortality rate, for which the greater severity of the condition may have been responsible, 30 prevesical prostatectomies with an insignificant mortality rate and numerous endoscopic resections.

On the basis of his personal experience he stated that endoscopic resection may be preferred to prevesical intervention for small prostatic neoformations. However, the high costs of instruments may present a major difficulty for more general use of endoscopic resection.

Perineal or prevesical intervention may be preferred for moderate prostatic enlargement, although the perineal method almost always causes impotencé and frequently causes urinary incontinence. Satisfactory results in general may be obtained with the prevesical technic. The transvesical prostatectomy in one or two stages should not be abandoned completely, because its immediate and late results are excellent, although it entails a longer period of recovery.

For larger prostatic neoformations, Professor Nicolich prefers transvesical prostatectomy in two stages.

Membranous Pericolitis and Pseudoappendicitis

In a meeting of the Neapolitan Society of Surgery Professor De Leo called attention to so-called pseudoappendicitis. Jackson's membrane is one of the causes of a congenital abnormality. It resembles a covering, cord or ribbon, which may be observed at the periphery of the intestinal tract from the terminal loop of the ileum to the transverse colon. Professor De Leo has observed such membranes in about 11 per cent of his patients for whom operations were performed after a diagnosis of appendicitis, and in 5 of 10 necropsies performed on persons who had died from digestive diseases. In contrast to this, the records of the Pilgrim Hospital in Naples revealed a death rate of approximately 0.6 per cent in 2,022 patients who had undergone appendectomy.

Professor De Leo suggests that the difference in statistics is due to confusion of Jackson's membrane with adhesions. The differentiation is important because inflammatory adhesions may recur after section or excision, whereas this does not occur with Jackson's membrane. Removal of inflammatory adhesion does not seem indicated, while removal of Jackson's membrane usually is recommended.

PARIS

(From Our Regular Correspondent)

July 10, 1949.

A New Sign of Death

Icard's process with fluorescin is at present considered the most certain means of ascertaining death. At one of the last meetings of the National Academy of Medicine, Prof. V. Balthazar proposed a process which he has used efficaciously for twenty-five years. In 1923, one of his disciples, Dr. Rebouillat, demonstrated that the subcutaneous injection of 1 to 2 cc. of ether is resorbed as long as a vestige of life persists, whereas, if death has occurred, ether spurts back when the needle is withdrawn. This process offers the advantage of being without danger for the subject in a state of apparent death, and it constitutes, at the same time, the first means of restoring the subject to life. Every time this sign has been positive, it has been impossible to reanimate the subject. This is important, as it permits one to proceed with autopsy and with the taking of grafts and other organs immediately after death (provided the subject is dead and there exists no possibility of reanimation) as authorized by the recent legal provisions. Professor Balthazar proposed the use of the "ether sign" especially in newborn infants, among whom apparent death is frequent, and he predicted that this new sign will replace all others in present use.

Fourth International Scientific Conference at Dax

The Fourth International Scientific Conference will take place in Dax Oct. 13-16, 1949, under the auspices of the International Society of Medical Hydrology and the French League Against Rheumatism (president Professor Portman, dean of the Bordeaux faculty of medicine). The subjects to be discussed are: (1) peloïds; (2) nontubercular hydrarthrosis of the knee; (3) hydrarthrosis of the knee and (*a*) gout, (*b*) syphilis, (*c*) tumors and (*d*) nervous arthropathies; (4) vascular disorders; (5) infectious pseudorheumatism; (6) progressive inflammatory chronic rheumatism; (7) arthrosis; (8) periarthritis; (9) endocrinian hydrarthrosis; (10) traumatic and nontraumatic hydrarthrosis; (11) hydrarthrosis of the knee in children; (12) biopsy and articular puncture in the diagnosis of hydrarthrosis of the knee, and (13) physical therapy, crenotherapy and medical and surgical treatment in hydrarthrosis. Sight-seeing trips are planned in Dax, Hossegor, Biarritz and St. Jean de Luz; there will also be a banquet. All communications should be addressed to: Commission médicale de la Guatrième Conférence Scientifique Internationale de Dax, Hotel Splendid Cours de Verdun, Dax (Landes), France.

BELGIUM

(From Our Regular Correspondent)

July 19, 1949.

Medicolegal Diagnosis of Alcoholic Intoxication

G. Kettenmeyer, who has been charged with making a report by the commission appointed to study the medicolegal diagnosis of alcoholic intoxication, has presented the results of these investigations to the Belgian Society of Legal Medicine.

Only the determination of alcohol in the blood gives maximum precision. The interpretation of the determination of the quantity of alcohol in other body fluids can give rise to disputes. Nevertheless, examination by a physician of persons supposedly in a state of intoxication is useful, and the result of these clinical determinations should be noted in a special observation blank, such as in use in the judiciary department of the district of Brussels. The physician concerned with the legal aspects who is in possession of these results will be able to estimate the degree of alcoholic intoxication.

The commission has decided that systematic medicochemical diagnosis of alcohol intoxication will be possible if withdrawal of blood is obligatory.

Professional Life

The Association of Professional Organizations of Specialists has been formed in Brussels to bring together Belgian professional organizations of medical specialists for (1) the study, protection and development of professional interests of medical specialists and (2) the study of conduct in the relationships of medical specialists with patients and colleagues and with diverse collective bodies and public authorities.

Atomic Research in Belgium

The University Institute of Nuclear Research—composed of selected specialists in the establishments of higher education in the country—has been charged with creating a center of atomic research which will be erected in a suitable locality. It is believed that the site is an isolated part of the Ardennes. This center will be made effective in 1950. It will be interested especially in the construction of an atomic pile and will be active in the production of radioactive isotopes.

MADRID

(From Our Regular Correspondent)

July 9, 1949.

Pharmacology and Therapeutics

The chair of pharmacology and therapeutics of the University of Madrid for many years was occupied by Dr. T. Hernando.

Among his former students are: Dr. T. Alday Redonnet, who has studied the pharmacology of digitalis; Dr. R. Méndez, formerly of the Department of Pharmacology, Loyola University, Chicago, but now with the Instituto de Cardiologia of México, and Dr. B. Lorenzo Velázquez, who occupies the chair formerly held by Dr. Hernando at the University of Madrid.

Included in the research at the University of Madrid is a study of the spasmolytic effect of sodium beta-glycerophosphate on the uterus and its analeptic effect on respiration. The intravenous injection of this substance causes decreased uterine hypertonicity. Obstetric clinics in Spain, Portugal, Italy, Cuba, Argentina and some other countries are using this substance. While studying procaine, researchers found that the etanolic diethyl-amino group inhibits cholinesterase whereas the benzoic para-amino group does not affect cholinesterase. They also found that procaine increases the effect of posterior pituitary injection so that only one third of the normal dose of the latter is needed with procaine if administered concurrently. Some of the studies seem to indicate that inhibition of the acetylcholinergic action occurs in narcosis.

Drs. Lorenzo Velázquez, Bayo and García de Jalon are studying a histolytic saphrophytic (nonpathogenic) bacterium which is found in the air. The results of some of the studies of Dr. Velázquez and his collaborators are published in *Farmacoterap. actual* (**55-56**:10) 1949. When this organism is planted in an aqueous medium with sodium glycerophosphate solution, 1:1,000, and histamine hydrochloride (10 cc. of sodium glycerophosphate solution to 1 cc. of histamine hydrochloride) the histamine disappears within eight or ten days. The histaminolytic action of the bacteria can be increased by passing them through blood agar. When the activated bacteria are planted again in the glycerophosphate histamine solution, inactivation of histamine occurs within eight or ten hours. The bacteria when planted in the culture medium liberate histaminase or an enzyme which destroys histamine. Dr. Meier of Basel and his associates also studied the same strain, which they obtained from Madrid. They identified histaminase in the filtrate of the bacterial cultures. This is an aerobic organism; and when the organism or the bacteriologic medium containing it is in contact with air it produces a large amount of histaminase which is highly thermolabile. The strain of the aforementioned bacteria will be sent to all scientific departments requesting it. The address is: Dr. B. Lorenzo Velázquez, Instituto de Farmacología, Facultad de Medicina, Atocha 104, Madrid, Spain.

Correspondence

DIAGNOSIS OF CANCER

To the Editor:—The editorial entitled "Diagnosis of Cancer" appearing on page 586 of THE JOURNAL, February 26, is disappointing. The writer failed to understand the spirit and stimulation of Dr. Greene's article in the *Scientific American*. This is evident in the first sentence, where the editor uses the word "deprecatory" to describe statements in Dr. Greene's article. Dr. Greene nowhere in his article disapproves of the standard and practical methods of diagnosis of cancer. What he does do is present a new tool for the study and appreciation of cancer. He points out that the bone of contention is the definition of cancer. If the method which he describes—that is, the heterologous transplantation method—will lead to a more accurate definition, it will be of extreme value, even if it proves to be of no value in any other respect.

The editorial writer calls for "proof," and yet he distorts the examples given in Dr. Greene's article to "prove" his own objections to the article. He constantly admits that errors can and have been made in determining malignancy by the routine microscopic examination, and yet he objects to a new method that may lead to a complete change in our concept of malignancy. The article was written for lay readers and therefore had to be written clearly and unequivocally. I doubt seriously that it undermines anybody's confidence in the medical profession; rather, I think, it does the opposite; it stimulates the public confidence that advances are being made in the field of cancer, with the hope of ultimate understanding and cure. The public is a great advocate of scientific advance and would probably object, I believe, to being called in as a dumb witness in condemnation of a first rate popular scientific article.

THOMAS N. MEREDITH, M.D., Pittsburgh.

COMMENT:—The editorial objected to certain quoted statements in a paper published in the *Scientific American*, December 1948, by Dr. Harry S. N. Greene. The objections were illustrated by four quotations from the article and were based on statements some of which were untrue, or partly true, or potentially misleading. These statements might cause unwarranted loss of confidence on the part of the public in one of the standard methods for diagnosing cancer—and this at a time when great efforts are being made to educate the public to have earlier diagnosis of cancer, by submitting to biopsy if necessary. A number of highly qualified persons after reading the article concurred in the opinions expressed by the editorial, and others have commented favorably after reading the editorial.

The editorial made no comment on the heterologous intraocular transplant test as an interesting, stimulating and perhaps important technic for studying the biology of neoplasms. It did object to its being advocated as a reliable test for cancer. For example, the statement (which was not quoted in the editorial) made on page 42, to the effect that "For the present, heterologous transplantation provides a reliable test for cancer," is false on the basis of evidence now available. A recent report in the literature (Eichwald, E. J.: Heterologous Transplantation of Cancer of Childhood, *Cancer Research* **8**:273 [June] 1948) found one successful "take" in 158 animals (1 case in 27 tests). The greatest degree of success that Greene has reported is 4 "takes" in 11 cases (Greene, H. S. N.: Heterologous Transplantation of Mammalian Tumors: II. The Transfer of Human Tumors to Alien Species, *J. Exper. Med.* **73**:475-486 [April] 1941). True, Greene later reported 10 successful takes, but he failed to state how many negative results he had during that same period (*Cancer Research* **4**:352 [June] 1944). On direct question as to how many positive cases he would have in 100 consecutive cases of cancer, Greene failed to reply (J. A. M. A. **137**:1364 [Aug. 14] 1948). There are other reports of negative results in the literature. Neither Greene nor others, therefore, have presented evidence that this is a reliable test for cancer. The evidence points to the contrary.

At the same time these data disprove Greene's statement (page 41) that . . . "It is significant that all tumors which possess the ability to invade and metastasize to other tissues in the body can be transplanted to animals of alien species . . . ." on the basis of his own published results.

Greene apparently wishes to redefine the word "cancer" (page 41). It would probably be better if he were to coin a new word to describe the ability to "take" after transplantation into the anterior chamber of an alien species. There would be no objection to this. It would permit the word "cancer" to be retained to signify a new growth of tissue which the body is unable successfully to bring under complete control. This tissue can invade, metastasize and kill the human host (conforming to the definition of cancer) even if it is not transplantable to an alien species.

As was stated by Dr. Meredith, the editorial used the word "deprecatory" in relation to certain statements of Greene. It is now apparent that a stronger word could have been justifiably used. The article in question contained not only statements which can be regarded as deprecatory to microscopic diagnosis of cancer, but statements which, on the basis of evidence now available, are untrue. The adverse influence which these statements might have on the public and on that segment of the medical profession which has not followed the developments in this special field of research is regretted.

BROMIDES, HYPOPHYSIS AND THYROID

To the Editor:—I have read the interesting article by Ravdin, Rose and James Maxwell, which appeared in THE JOURNAL (**140**:141-146 [May 14] 1949) under the heading "The Treatment of Thyrotoxicosis." With respect to the first part of that article, in which various treatments of thyrotoxicosis are dealt with, I wish to call the attention to the action of bromides (sodium bromide) on the thyroid and the hypophysis.

In a group of researches (worked out from 1934 to 1943, *Arch. di fisiol.*, 1939-1940; *Boll. Soc. ital. biol. sper.* 1936, 1939

and 1943; *Naturwissen.*, 1938-1940; *Riv. Svizzera di Med.*, 1940), my co-workers and I showed that sodium bromide when administered for a long period and in proper doses to animals (dogs, rabbits, rats) causes a remarkable decrease in the iodine content of the thyroid and, consequently, evident hypofunction of this gland. This is physiologically proved by a decrease of basal metabolism, arrest of growth in young animals and so forth.

Bromide causes also a hypofunction of the hypophysis. These observations are somewhat in accord with G. Deltour's views (*Presse méd.* **25**:42, 1949) according to which "the ideal antithyroid agent would be that which would have an inhibitory action on the thyroid secretion and on the hypophysis."

The investigations hitherto carried out by my co-workers and me have purely an experimental character. Nevertheless, we do not deny that they may find clinical application, as we maintain, based on experimental data, that bromide is to be considered a substance with an antithyroidal action even if the details of the mechanism of action are not yet clear.

GIOVANNI MORUZZI
Istituto di Biochimica
University of Bologna

IN SUPPORT OF HYGEIA

To the Editor:—Although I have been out of medical school for more than five years, I have only recently become acquainted with *Hygeia* magazine. The attention of all doctors should be called to the valuable service this periodical can perform for them if their patients read it. The articles give the patients the sort of knowledge we find in our medically well educated patients and try to impart with considerable pains to our less well educated patients; yet the information given never invades the doctor's province—unlike medical articles in almost all other periodicals. We doctors can save ourselves much time and energy and facilitate instruction in health preservation by urging all our patients to subscribe to and read *Hygeia* thoroughly.

ARTHUR F. GREENWALD, M.D., Los Angeles.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY, INC. *Oral.* Denver, Oct. 16-20. Sec., Dr. Curtiss B. Hickcox, 745 Fifth Ave., New York 27.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY, INC.: *Oral.* Cincinnati, Oct. 21-23. Sec., Dr. George M. Lewis, 66 East 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 17. Asst. Sec.-Treas. Dr. W. A. Werrell, 1 Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 3. Final date for filing applications is Jan. 1. Sec., Dr. W. J. German, 789 Howard Ave., New Haven.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC. *Part I.* Various Centers. Feb. 3. Final date for filing application is Nov. 5. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, Oct. 15-19; Boston, April. Sec., Dr. Edwin B. Dunphy, 56 Ivie Rd., Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY. *Part II.* New York City, Feb. 9-10. Address: Sec.-Treas., Dr. Harold A. Sofield, Room 1856, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 4-7. Sec., Dr. D. M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Chicago, Oct. 7-8. Sec., Dr. Robert A. Moore, 507 Euclid Ave., St. Louis.

AMERICAN BOARD OF PEDIATRICS: New York City, Oct. 21-23; Chicago, Dec. 9-11. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: Examinations are given in June and November of each year in the home town of applicants. Sec.-Treas., Dr. Louis T. Byars, 400 Metropolitan Bldg., St. Louis, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: *Parts I and II.* New York, Oct. 22-24. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY: November. Sec., Dr. Louis A Buie, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC. *Special Examination.* Chicago, Oct. 24-25. December, New York City. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Cincinnati, Sept. 28-Oct. 2. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, October 26 Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Written.* December. *Oral and Clinical.* Chicago, Feb. 11-15. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 18.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 27-29. Sec., Dr. D. G. Gill, 519 Dexter Avenue, Montgomery.

ARKANSAS: * *Examination.* Little Rock, Nov. 3-4. Sec., Dr. Joe Verser, Harrisburg. *Eclectic.* Little Rock, Nov. 3. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

COLORADO: * *Endorsement.* Denver, Oct. 4. Sec., Dr. George H. Gillen, 831 Republic Building, Denver.

CONNECTICUT: * *Examination.* Hartford, Nov. 8-9. Secretary to the Board, Dr. Creighton Barker, 160 St. Ronan Street, New Haven.

DELAWARE: *Examination.* Dover, Jan. 10-12. *Reciprocity.* Dover, Jan. 19. Sec., Dr. J. S. McDaniel, 229 State Street, Dover.

DISTRICT OF COLUMBIA: * *Examination.* Washington, Nov. 14-15. Sec., Dr. G. C. Ruhland, 4130 E. Municipal Bldg., Washington.

FLORIDA: * *Examination.* Jacksonville, Nov. 27-29. Sec., Dr. Frank D. Gray, 12 N. Rosalind Ave., Orlando.

GEORGIA: *Examination.* Atlanta, Oct. 11-12. *Reciprocity.* Atlanta, Oct. 13. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

GUAM: *Endorsement.* Agana, Last Friday of each month. Sec., Capt. C. K. Youngkin, Dept. of Public Health, Guam, % F.P.O., San Francisco.

IDAHO: Boise, Jan. 9. Exec. Sec., Mr. Armand L. Bird, 305 Sun Building, Boise.

ILLINOIS: Chicago, Oct. 4-6. Supt. of Registration, Mr. Fred W. Ruegg, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June. Sec., Dr. Paul R. Tindall, 1138 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Des Moines, Dec. 5-7. *Reciprocity.* Des Moines, Oct. 3, Nov. 7, Dec. 5. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Topeka, Dec. 8-9. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

MAINE: Portland, Nov. 8-9. Sec., Dr. Adam P. Leighton, 192 State Street, Portland.

MARYLAND: *Examination.* Baltimore, Dec. 13-16. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1. *Homeopathic. Examination.* Baltimore, Dec. 13-14. Sec., Dr. John A. Evans, 612 West 40th St., Baltimore.

MINNESOTA: * Oct. 18-19. Sec., Dr. Julian F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity.* Jackson, December. Sec., Dr. Felix J. Underwood, State Board of Health, Jackson 113.

MISSOURI: *Examination.* Jefferson City, October 24-26. *Reciprocity.* Jefferson City, October, 23. Exec. Sec., Mr. John A. Hailey, State Capitol Building, Jefferson City.

MONTANA: Helena, Oct. 3-5. Sec., Dr. Otto G. Klein, First National Bank Bldg., Helena.

NEVADA: Carson City, Nov. 7. Sec., Dr. George H. Ross, 112 N. Curry St., Carson City.

NEW JERSEY: Oct. 18-21. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe. Oct. 10-11. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

NEW YORK: *Examination.* New York, Albany, Syracuse and Buffalo, Oct. 4-7. Sec., Dr. Jacob L. Lochner Jr., 23 S. Pearl St., Albany 7.

NORTH CAROLINA: *Endorsement.* Asheville, Oct. 17. Sec., Dr. Ivan Proctor, 226 Hillsboro Street, Raleigh.

OHIO: *Examination.* Columbus, December. *Endorsement.* Oct. 2. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OREGON: *Endorsement.* Portland, Nov. 4-9. Exec. Sec., Mr. Howard I. Bobbitt, 608 Failing Building, Portland.

OKLAHOMA: * *Examination.* Oklahoma City, June 7-8. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

PENNSYLVANIA: *Examination.* Philadelphia or Harrisburg, January. Acting Sec., Mrs. Marguerite G. Steiner, 351 Education Buliding, Harrisburg.

RHODE ISLAND: * *Examination.* Providence, Oct. 6-7. Chief, Mr. Thomas B. Casey, 366 State Office Building, Providence.

SOUTH CAROLINA: *Examination.* Columbia, Nov. 8-9. *Reciprocity.* First Monday of every month. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Sioux Falls, Jan. 17. Sec., Dr. C. E. Sherwood, 300 First National Bank Building, Sioux Falls.

TENNESSEE: * *Examination.* Memphis, Sept. 28-29. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

VIRGINIA: *Examination.* Richmond, Dec. 2-3. *Reciprocity.* Richmond, Dec. 1. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

WASHINGTON: * Seattle, January. Director, Department of Licenses, Mr. Edward C. Dohm, Olympia.

WEST VIRGINIA: *Examination.* Charleston, Oct. 3-5. *Reciprocity.* Charleston, Oct. 3. Director, State Health Department, Dr. N. H. Dyer, Room 639, Capitol Building, Charleston.

WISCONSIN: * *Examination.* Madison, Jan. 10-12. Sec., Dr. C. A. Dawson, River Falls.

WYOMING: Cheyenne, Oct. 3. Sec., Dr. Franklin D. Yoder, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Examination.* Tucson, Sept. 20. Sec., Mr. Francis A. Roy, Science Hall, University of Arizona, Tucson.

ARKANSAS: *Examination.* Little Rock, Oct. 4. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.

CONNECTICUT: New Haven, Oct. 8. Executive Assistant, State Board of Healing Arts, Miss Mary G. Reynolds, 110 Whitney Ave., New Haven 10.

DISTRICT OF COLUMBIA: Washington, Oct. 24-25. Sec., Dr. G. C. Ruhland, 4130 E. Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, Nov. 5. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Oct. 14-15. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing 15.

MINNESOTA: *Examination.* Minneapolis, Oct. 4-5. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, Oct. 4-5. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln 9.

OKLAHOMA: *Examination.* Oklahoma City, April 11. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

OREGON: Portland, Dec. 3. Sec., Mr. Charles D. Byrne, State Board of Higher Education, Eugene.

SOUTH DAKOTA: Vermillion, Dec. 2-3. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

WASHINGTON: Seattle, January. Director, Department of Licenses, Mr. Edward C. Dohm, Olympia.

WISCONSIN: Milwaukee, Sept. 24 and Dec 3. Sec., Prof. W. H. Barber, Ripon College, Ripon.

Medical Motion Pictures

FILM REVIEWS

The following 16 mm., black and white, silent motion pictures are a series of psychiatric films on Integrated Development: Studies of the Interaction between children and their environment. Prepared by Margaret E. Fries, M.D., and her collaborators at the New York Infirmary for Women and Children. Procurable on rental or purchase from the New York University Film Library, 26 Washington Place, New York 3.

Some Basic Differences in Newborn Infants During the Lying-In Period. 540 feet (2 reels), showing time twenty-two minutes. Produced in 1944.

This film attempts to illustrate the differential behavior responses to standard stimuli among three "types" of newborn babies: the "active," the "moderately active" and the "quiet." In one test a weight is dropped from a constant height at a given distance from the child; another test is based on suckling and withdrawal of the breast for intervals of one minute each. According to the film one "type" of child will always respond to startle or deprivation with restless activity, another with passive resignation or sleep and a third with patterns of reaction somewhere between these extremes. The film implies, moreover, that these innate patterns remain constant for life.

The picture illustrates that children differ in neuromuscular integration and development at birth, but neither the scenes nor the subtitles clarify the issue as to whether such differences are attributable to varying rates of intrauterine growth or simply to the length of time between conception and delivery. The final sections of the film show that a mother's attitudes toward her infant may be revealed in the way she nurses it, for example, with uncomfortable tension, with ambivalent overconcern or with affectionate warmth and mutual pleasure. A final somewhat adventitious subtitle informs all adults that "we must accept children as they are."

This film is suitable for showing to residents in pediatrics and students in medicine and psychology.

The photography and editing of this film are acceptable, but, as indicated, the classification of mothers and children into simple categories is arbitrary and possibly misleading.

Psychological Implications of Behavior During the Clinical Visit. 400 feet, showing time sixteen minutes. Produced in 1944.

The introductory sequences of this film show various ways in which mothers hold and nurse their infants, for example, with tense, mutual discomfort, with smothering physical effusiveness or with relaxed and protective warmth. Later scenes in the film show how the play activities of older children can express jealousy, hostility, avoidance of anticipated rejection, anxious possessiveness, compensatory identifications with other children or trusted adults or fearful withdrawal. A final subtitle somewhat redundantly confirms the fact that each child has a unique personality derived from his individual development and experiences.

This film may be useful as an adjunct for lectures to lay groups on maternal care and child development.

A Psychoneurosis with Compulsive Trends in the Making: Life History of Mary. 1,100 feet (4 reels), showing time forty-six minutes. Produced in 1947.

Lying-In Period.—The film begins by classifying its child heroine, Mary, as a "congenital active type" on the basis that startling stimuli even a few hours after birth produce crying and restless seeking. Mary's mother dislikes nursing her and is compulsive and ritualistic in her care. The contrast is heightened by interpolation in the film of scenes showing the nursing procedures of a truly affectionate mother, but the issue at this point is somewhat obscured by a series of subtitles giving arbitrary descriptions of the characteristics of other members of Mary's immediate family.

Mary's Life from 2 Weeks to 2 Years.—This section of the film shows how the infant Mary becomes increasingly insecure and tense as she senses her mother's ambivalence and is subjected to successive deprivation, such as early weaning and premature discipline. She turns to her father for help but, although he reciprocates her affection, she becomes a somber, anxious child whose main defenses against unhappiness consist of intellectual pretentions and channelized hyperactivity. Despite Dr. Fries' attempt to guide Mary's mother, Mary seems already to be fulfilling an earlier prognosis that she would develop an anxiety neurosis with obsessive-compulsive traits.

Mary from 2 to 7 Years.—During this age range Mary continues to show diminished frustration tolerances, in that she withdraws from play situations into ritualized activities or displaces her aggressions onto dolls or other inanimate objects. At times her overt hostilities break through into overt behavior, such as resistiveness to discipline or physical destructiveness, but for the most part she is an excessively inhibited, timid and compulsive child.

By the time Mary is 5 years old she has a decided handwashing compulsion and a susceptibility to disabling anxiety whenever her ritualistic habits are interfered with. Her posture is poor, and, despite her superior intelligence quotient, she is retarded in intellectual and motor development Her social development is correspondingly impaired, so that she has no friends and few of the skills and graces essential for group acceptance.

This film is a poignant documentary of the familial and childhood deprivations that can threaten the happiness and usefulness of a lifetime; moreover, it emphasizes how little can be done by child psychiatrists who, though aware of the concurrent tragedy, are not given the psychiatric and social means with which to alter the outcome.

The film is recommended for exhibition to students of medicine, nursing, social work and psychology as well as to lay groups interested in child behavior.

The Family Life of the Navaho Indians. 630 feet (2 reels), showing time twenty-six minutes. Produced in 1944.

This film records some of the child-rearing customs of a Navaho tribe. If the film has a point, it is that the Navaho infant though nearly always kept strapped into immobility on a cradle board derives great security from the continuous attentions showered on him by his mother and older siblings. The little Navaho girl is given duties about the hogan and the farm plot at an early age, whereas the Navaho boy is

encouraged to acquire skill in horsemanship and native crafts. Both are thus made to feel accepted into the community when young, presumably for the good of all concerned.

The film is a pleasant documentary and may serve as a text for more penetrating discussions of cultural influences on personal and social development.

The Diagnosis and Treatment of Leukorrhea, A Clinical Presentation. 16 mm., sound, color, 1,400 feet (1 reel), showing time thirty-eight minutes. Prepared in 1947 with the cooperation of William Bickers, M.D., Richmond, Va. Produced by Springer. Sponsored by and procurable on loan from Ciba Pharmaceutical Products, Summit, N. J.

This film presents an outline of the etiologic aspects and treatment of leukorrhea. The various pathologic conditions of the cervix and vaginal mucosa as well as conditions which produce vaginal discharge and the underlying pathologic conditions are well illustrated. Several patients are shown, and the various forms of this condition and treatment are described for each case. Charts are used to depict the classification of cases of leukorrhea found in office practice.

This film has little teaching value, since a number of statements and presentations undoubtedly will be questioned by the more meticulous practitioners of gynecology. One is left with the impression that all vaginal discharges can be cured by insufflation with vioform® (5-chloro-7-iodo-8-hydroxyquinoline) and that such treatment is practically devoid of danger. The film might better have referred to "one method of treatment" instead of implying that "this is the treatment."

The color photography and narration are excellent.

The production is long, and judicious editing would be an improvement; for example, the scene of the patient walking to the physician's office is hardly necessary.

Cardiac Arrhythmias. 16 mm., color, silent, 600 feet (1 reel), showing time twenty-five minutes. Prepared in 1948-1949 by Robert Shuler, Ph.D., M.D., with assistance from Mark F. Hanch, M.D.; Richard Shaw, M.D., and David MacDougal, M.D., University of Chicago, Department of Physiology, Chicago. Procurable on loan from Abbott Laboratories, North Chicago, Ill.

The valuable portion of this film is the series of scenes showing the exposed canine heart in arrhythmias of various kinds, experimentally produced. These are supplemented by animated diagrams and by schematic electrocardiograms. The purpose of the film is to give the clinician a clearer understanding of arrhythmias that are observed in patients.

The animation of the spread of the excitation wave was extremely diagrammatic and sketchy and could be interpreted as inacurrate in at least three instances when the impulse was shown to travel (*a*) down the septum from the base to the apex and (*b*) up the walls of the ventricles from the apex to the base and (*c*) when the recession of the excitation wave was said to account for the T wave formation, whereas it is now considered by many that our previous acceptance of this possibility is no longer certain, although it might possibly be assumed, as a working hypothesis. The film correctly depicts auricular fibrillation as being caused by the activation of multiple foci in the auricles in accordance with a rather recent change in our understanding of the production of this arrhythmia. However, it is rather difficult to think of auricular fibrillation without recalling the older theory of "circus movement," and possibly this theory should have been mentioned.

The normal ryhthm, 2 to 1 and 3 to 1 heart block; auriculoventricular nodal rhythm; complete auriculoventricular block; auricular fibrillation and flutter; ventricular fibrillation, and paroxysmal ventricular tachycardia are shown. These arrhythmias are shown as they occur in experimental animals and are repeated with animation of the diagrammatic heart and the simultaneous production of the electrocardiogram. The animation was rather jerky over the auricles when traveling over the normal pathways. Auricular flutter was beautifully shown as a ripple of contraction continuously moving around the appendage of the left auricle. In the depiction of the electrocardiogram of ventricular fibrillation, a poor curve is used. Obviously a dog's heart in extremis was photographed and showed the fibrillatory movements well. In the photography representing paroxysmal ventricular tachycardia, the auricles were seen to be beating independently at a slower rate, which probably occurs only in the presence of complete heart block.

Most of the arrhythmias are mentioned. Ventricular escape is omitted, but the admixture of skimpy diagrams and the nearly complete coverage of the subject makes it difficult to know to whom the film is directed. Certainly this film is not for the medical student, because the sketchiness of the conduction system and the improper manner of spread of the excitation impulse are unsatisfactory.

The strongest point of the film is the excellent photography of the dog's heart.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Books: Admissibility in Evidence.—The defendant, charged with poisoning his wife with strychnine, was found guilty by a jury and convicted of murder in the first degree. From such conviction, he appealed to the Court of Appeals of New York.

Among other reasons cited by the Court of Appeals for requiring a new trial, it was held that the conviction would have to be reversed because of the trial court's ruling on the right of the defendant to cross examine one of the expert witnesses. When a toxicologist, a witness for the state, was being cross examined, the following questions were asked of him:

Q. Now, you said that you got part of your information or knowledge about toxicology from literature; is that right?

A. That's right.

Q. Did you ever read "Textbook of Physiology" by Howell?

A. I've glanced at it.

The trial court, without more, then ruled that if counsel wished to refer to any textbook or literature he must show it to the witness and that if the witness agreed with it and adopted it, the witness might then be questioned about it. The trial court said, " . . . I shall not permit you to read from that book or any other book. If you wish to question this witness regarding any material, any writing, any dissertation or questions or statements contained in that book, you will first refer to the witness; let him read it, and, if the witness replies that he is in agreement with it or that he adopts that argument as his own, then I will allow you to make reference to it. Otherwise, not." Later during the same discussion the trial court repeated the ruling as follows: " . . . you will first refer the book to this witness, and, if the witness tells the Court that he is in agreement with that statement or that writing and adopts that argument as his own, you may then question him regarding such statement or such argument. Otherwise I shall exclude it."

In this state, said the Court of Appeals, when an expert witness has given opinion testimony and on cross examination has tesified that a book called to his attention is recognized by him as an authority on the subject on which he has given an opinion, he may be confronted with a passage from the book which conflicts with the opinion he has expressed. This is permitted for the purpose of discrediting or weakening his testimony. In a prior New York case it was said: " . . . it has been the custom, in this state at least, to call the attention of expert witnessess, on cross examination, to books on the subject and ask whether or not authors whom he admitted to be good authority had not expressed opinions different from that which was given by him upon the stand. The reference to books in such cases is not made for the purpose of making the statements in the books evidence before a jury, but solely for the purpose of ascertaining the weight to be given to the the tesimony of the witness."

Accordingly the defendant's conviction was reversed and a new trial ordered. *People v. Feldman 85 N. E. (2d) 913 (New York, 1949).*

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1938 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

19:301-400 (April) 1949

SYMPOSIUM ON THE CYTOLOGIC DIAGNOSIS OF CANCER

Cytologic Diagnosis of Uterine Cancer by Examination of Vaginal and Uterine Secretions. G. N. Papanicolaou.—p. 301.
Cytologic Diagnosis of Cancer from Pleural and Peritoneal Fluids. O. Saphir.—p. 309.
Cytologic Diagnosis of Carcinoma of the Prostate. P. A. Herbut. —p. 315.
*Tumor Cells in Bronchial Secretions: Experimental and Statistical Study. M. Appel and T. T. Bronk.—p. 320.
Cytohistologic Study of Bronchial Secretions. H. L. Richardson, W. C. Hunter, W. S. Conklin and A. B. Petersen.—p. 323.
*Cytohistologic Diagnosis of Material Aspirated from Stomach; Accuracy of Diagnosis of Cancer, Ulcer and Gastritis from Paraffin-Embedded Washings. H. L. Richardson, F. B. Queen and F. H. Bishop.—p. 328.

Tumor Cells in Bronchial Secretions.—Appel and Bronk report a woman aged 58 with paroxysmal attacks of dyspnea, associated with cough and loss of weight. Repeated roentgenographic examinations of the chest did not reveal a neoplasm. Bronchoscopy showed no evidence of tumor. Clusters of tumor cells were observed in secretions obtained from the right main bronchus and stained by the Papanicolaou technic. Pneumonectomy was performed. Careful dissection of the bronchial tree revealed a small area of thickening occluding a tertiary division of the right bronchus. Microscopic sections of this area showed papillary projections of a primary carcinoma arising in the bronchial mucosa. Despite the small size of the primary tumor, there was sufficient exfoliation of tumor cells to make them readily recognizable in the bronchial secretions before there was any definite clinical, roentgenologic or bronchoscopic evidence of tumor. Experiments on 30 rabbits in which pulmonary carcinomas were produced by transplantation of a tumor of the testis of the rabbit revealed exfoliated cells in the bronchial secretions in all the animals. In 17 animals tumor cells could be found in the bronchial secretions before the tumor was grossly recognizable and at a stage at which neither roentgen examination nor bronchoscopy could have identified the growth.

Cytohistology of Gastric Washings.—Richardson and co-workers embedded in paraffin and sectioned material from 297 gastric aspirations obtained from 235 patients. The sections contained not only isolated cells but also frequently minute fragments of tissue. Consequently, the term "cytohistologic" was applied to this method of diagnosis. In 136 patients the clinical diagnosis was not established beyond doubt, while 99 patients had proved lesions. In 78 of the latter group the diagnosis was proved at operation or autopsy, or by clinical observations and course. The proved diagnosis was compared with the cytohistologic diagnosis. The criteria for the cytohistologic diagnosis of cancer were clusters of enlarged, irregular cells with hyperchromatic nuclei and prominent nuclei; those of ulcers were fibrin mass containing enmeshed leukocytes; those of acute gastritis were many intracytoplasmic granulocytes in mucosal epithelium. Twenty-seven patients had proved cancer. In 13 the disease was originally diagnosed cytohistologically as cancer. On review of the sections, a total of 18 were given a diagnosis of cancer. A false-positive diagnosis of cancer was made in 2 patients. Twenty-four patients had proved ulcers. In 20 the diagnosis of ulcer was made from the microscopic examination. A false-positive diagnosis of ulcer was made in 3 patients. Nine patients had proved gastritis. Six were given the diagnosis of gastritis. A false-positive diagnosis of gastritis was made in 3 patients. Eighteen patients were proved to have no gastric lesions. In 11 this had been the diagnosis. Six persons were incorrectly called normal. The embedded section technic presents certain advantages over the smear technic, important among which are the concentration of material and the better preservation of cellular relationships.

American Journal of Diseases of Children, Chicago

76:227-364 (Sept.) 1949

Diagnostic Application of Study of Bone Marrow in Infants and in Children. H. G. Poncher.—p. 227.
Gargoylism: II. Study of Pathologic Lesions and Clinical Review of 12 Cases. S. Lindsay, W. A. Reilly, T. J. Gotham and R. Skaben. —p. 239.
Experimental Toxoplasmosis: I. Transmission of Infection in Utero and Through Milk of Lactating Female Mice. H. Eichenwald.—p. 307.

American Journal of Medical Sciences, Philadelphia

217:361-474 (April) 1949

*Why Are Fever Temperatures Over 106 F. Rare? E. F. DuBois. —p. 361.
*Major Surgical Operations in Presence of Bundle Branch Block: Study of Operative Risk in 59 Patients. P. H. Pfeiffer and J. S. La Due. —p. 369.
Effect of Roentgen Radiation on Production of Thoracic Duct Lymphocytes. W. N. Valentine, C. G. Craddock and J. S. Lawrence.—p. 379.
Congenital Hemolytic Jaundice in a Negro Family. J. Churg and M. Rosenbaum.—p. 383.
Blood Volume Studies in Middle-Aged and Elderly Males. J. E. Cohns and N. W. Shock.—p. 388.
Heart in Funnel-Shaped and Flat Chests. A. M. Master and J. Stone. —p. 392.
Value of Laboratory in Diagnosis of Poliomyelitis. M. J. Fox and H. E. Wallace.—p. 401.
Electro-Narcosis: Results in 125 Patients with Psychosis or Psychoneurosis. D. Goldman.—p. 405.
Studies upon Relation Between Plasma Antithrombin and Heparin. I. Influence of Plasma Antithrombin on Prothrombin Time. C. A. Tanturi and N. C. Wetzel.—p. 410.
Effect of Streptomycin on Blood Clotting Time and Prothrombin Time in Man. L. Elson.—p. 421.
Control of Dicumarol Therapy. J. H. Olwin.—p. 427.
Prognosis of Pneumonia. W. W. G. Maclachlan, M. M. Bracken and W. R. Bailey Jr.—p. 438.
Effect of Liver Dysfunction on Response to Dicumarol. E. H. Reisner Jr., J. Norman, W. W. Field and R. Brown.—p. 445.
Clinical Evaluation of New Liver Function Test, Colloidal Red Test, in Comparison with Thymol Turbidity Test. H. A. Strade and L. B. Dotti.—p. 448.
Treatment of Scleroderma. H. Beerman and J. H. Stokes.—p. 453.
The Overmedicated Nasal Cavity. N. D. Fabricant.—p. 462.

Fever Temperatures.—According to DuBois there is still much to be learned about temperature regulation in health and even more about fever. Little is known regarding the details of the chemical, electrical and physical reactions which occur in the hypothalamus and skin in response to changes in temperature. It is by delicate adjustments in these tissues that the balance between heat loss and heat production is maintained. A survey was made of 1,761 temperature readings in 357 patients suffering from diseases characterized by high grade fever. Only 4.3 per cent of the temperatures were above 106 F. (41.1 C.) None was above 107.8 F. (42 C.). In these fevers 608 readings were between 104 and 105 F. (40.0 to 40.6 C.). Less than half as many fell between 102 and 103 F. (38.9 to 39.4 C.). These are indications that in these fevers the "thermostat level" for the temperature-regulating mechanism was set in the neighborhood of 104 and 105 F. Temperatures much higher than 106 F. can be found in several conditions other than infectious diseases. The normal temperature-regulating mechanism may be overwhelmed suddenly by a fever cabinet or gradually by heat stroke with its exhaustion of the sweat glands. The mechanism together with the peripheral circulation often fails in moribund patients. Except for these anomalous conditions temperatures are kept safely below the danger level by an "emergency regulatory mechanism in fever" which acts chiefly through the peripheral circulation and the sweat glands.

Surgical Operations in Presence of Bundle Branch Block.—Pfeiffer and La Due investigated the surgical risk in 59 patients with bundle branch block who were subjected to major operations. Two patients died ten and sixteen days postoperatively of medical complications, a 3.3 per cent operative mortality to which the presence of heart disease presumably contributed. The total operative mortality, including strictly surgical complications, was 10 per cent. Although it was not

possible to get a comparable series of patients of the same average age (66.6 years) as the patients studied, the authors were able to obtain the operative mortality statistics on 260 patients 70 and 71 years of age who underwent subtotal gastric resections. In these 260 patients the average mortality was 3.4 per cent. Thus the presence of bundle branch block in itself does not constitute a contraindication to surgical intervention. Careful classification of heart disease and study of the functioning of other systems are of greater importance in evaluating operative risk. Postoperative complications did not appear to be more frequent or severe than might be expected for a comparable group of patients in the same age group.

American Journal of Physiology, Baltimore

156:1-136 (Jan.) 1949

Comparative Effects on Circulatory System of Positive and Negative Accelerations: Marey "Law." S. W. Britton.—p. 1.
Estimation of Relative Corpuscle and Serum Volumes in Blood by Various Applications of Dilution Principle. P. L. McLain and C. H. W. Rube.—p. 12.
Studies in Intracardiac Electrography in Man: III. Displacement of Cardiac Pacemaker. H. D. Levine, H. K. Hellems, J. W. Dow and J. F. Gowdey.—p. 19.
Acute Effects upon Lungs of Dogs of Large Intravenous Doses of Alpha-Naphthyl Thiourea (ANTU). C. K. Drinker and E. Hardenbergh.—p. 35.
Effect of Anoxic Anoxia on Myoglobin Concentration in Striated Muscle. W. E. Poel.—p. 44.
Efficiency of Various Types of Artificial Respiration at High Altitudes. F. R. Blood and F. E. D'Amour.—p. 52.
Further Observations on Depression of Renal Function Following Hypophysectomy. H. L. White, P. Heinbecker and D. Rolf.—p. 67.
Nephro-Omentopexy, Compensatory Renal Hyperfunction and Parallel Measurements of Renal Dynamics. N. S. R. Maluf.—p. 79.
Lactic and Pyruvic Acids in Blood After Glucose and Exercise in Diabetes Mellitus. M. K. Horwitt, O. W. Hills and O. Kreisler. —p. 92.
Possible Role of Skin in Effect of Adrenalin on Body Temperature and Respiratory Metabolism. C. E. Whitcher and F. R. Griffith Jr. —p. 114.
Experimental Production of Electrical Major Convulsive Patterns. A. M. Freedman, P. D. Bales, A. Willis and H. E. Himwich.—p. 117.
Di-Isopropyl Fluorophosphate: Site of Injection and Variation in Response. A. M. Freedman and H. E. Himwich.—p. 125.
Water, Nitrogen and Electrolyte Content of Brain Following Cerebral Concussion. L. Eichelberger, J. J. Kollros and A. E. Walker. —p. 129.

American Journal of Psychiatry, New York

105:721-800 (April) 1949

Role of Medical Administration of Psychiatric Hospital Treatment. W. L. Russell.—p. 721.
*Transorbital Lobotomy. W. Freeman.—p. 734.
New Instrument for Performing Transorbital Leukotomy. M. T. Moore. —p. 741.
*Frontal Lobotomy: Clinical Experience with 107 Cases in State Hospital. J. E. Oltman, B. S. Brody, S. Friedman and W. F. Green. —p. 742.
Effects of Prefrontal Lobotomy on Symptomatology of Schizophrenic Patients: Survey of 100 Cases. D. Rothschild and A. Kaye.—p. 752.
Rating Scale Analysis of Clinical Effects of Lobotomy. S. L. Sands and W. Malamud.—p. 760.
Current Evaluation of Anticonvulsant Drugs. R. N. DeJong.—p. 767.
Practice of Psychiatry in Rural Community. J. Sirkin.—p. 775.
Reactions of Children to Highly Publicized Crime Against Child. S. S. Sloman.—p. 779.

Transorbital Lobotomy.—Transorbital lobotomy was originally proposed by Fiamberit in 1937. Preliminary studies on cadavers convinced Freeman that transorbital lobotomy is simple and quick. He employed this method on 10 patients early in 1946. The total number operated on by the transorbital method under his supervision has been about 100. Convalescence is rapid, many patients being discharged within a week. Some never manifest any improvement, and a few of these have subsequently undergone standard prefrontal lobotomy with good results. Although not all patients have been benefited, none has suffered aggravation of the mental condition as the result of the operative procedure. It has been particularly gratifying to find preservation of normal personality patterns in patients who have recovered. None of the inertia, indifference and indolence has been manifested; nor has there been the tactless, explosive or outspoken behavior noted so frequently following prefrontal lobotomy. Sometimes the adaptation of the patients is better than it was in their prepsychotic state. Transorbital lobotomy accomplishes much the same effect as topectomy of areas 9 and 10, in that it abates the psychosis without producing any undesirable personality changes. Transorbital lobotomy is simple, quick and safe. It is recommended particularly to psychiatrists in mental hospitals where major neurosurgical procedures are not available. Transorbital lobotomy under electroconvulsive shock should be undertaken when active therapy fails or is about to be replaced by "maintenance therapy." It should be definitely understood that the procedure is a minor one and that some patients may later require major lobotomy for permanent relief.

Frontal Lobotomy.—Oltman and associates review observations in 107 cases in which frontal lobotomy was performed at the Fairfield State Hospital in Newton, Conn. The group was composed almost entirely of patients with chronic mental illness whose prognosis seemed extremely unfavorable; 85 per cent were schizophrenic. The average duration of mental illness was 7.4 years and of hospitalization, 4.4 years prior to operation. The results following lobotomy have been encouraging: 56.7 per cent of the entire group exhibited significant improvement; thus far, 37.4 per cent have been able to leave the hospital. The mortality rate was low; complications, except for convulsive seizures, have been relatively infrequent. Results were best in the nonschizophrenic group, next best in the paranoid, catatonic and mixed types of schizophrenia, and poorest in simple and hebephrenic dementia praecox. Disturbed, aggressive, combative and hostile patients appeared to receive maximum benefit. Duration of illness had relatively little significance as a prognostic guide. Lobotomy may be especially helpful in patients who have pulmonary tuberculosis, which is a contraindication to shock therapy. There is no reduction of intellectual functioning after the operation.

American Review of Tuberculosis, New York

59:223-352 (March) 1949

Chemotherapeutic Measures in Tuberculosis: General Assessment and Current Problems. P. D'A. Hart.—p. 223.
Thoracoscopy and Closed Intrapleural Pneumonolysis. O. C. Brantigan. —p. 240.
Diagnostic Problem of Primary Pleural Effusions. J. R. Kraft.—p. 259.
Pulmonary Emphysema and Ventilation Measurements in 100 Anthracite Coal Miners with Respiratory Complaints. H. L. Motley, L. P. Lang and B. Gordon.—p. 270.
Management of Tuberculosis in Psychotic Patients. L. O. Lambiotte, E. L. Washington and G. S. Bozalis.—p. 289.
Fulminant Tuberculous Septicemia with Leukopenia. W. Pagel and A. L. Woolf.—p. 311.
Agranulocytosis During Streptomycin Treatment of Miliary Tuberculosis: Report of Case. D. D. Feld.—p. 317.
Direct Method of Standardizing Dilute Suspensions of Tubercle Bacilli by Use of Capillary Micropipette. W. D. Crandall.—p. 325.
Factors Affecting Sensitivity in Vitro of Tubercle Bacilli to Streptomycin. Elizabeth H. Williston and G. P. Youmans.—p. 336.

Anesthesiology, New York

10:125-246 (March) 1949

Studies of Circulation of Anesthetized Patients by New Method for Recording Arterial Pressure and Pressure Pulse Contours. K. F. Eather, L. H. Peterson and R. D. Dripps.—p. 125.
*Utility of Intravenous Procaine in Anesthetic Management of Cardiac Disturbances. C. L. Burstein.—p. 133.
Venous Pressure in Relation to Blood Volume in Man. M. E. Anderson Jr. and J. S. Lundy.—p. 145.
Some Observations upon Effect of Certain Anesthetic Agents on Uterine Motility During Labor. J. P. Howard, V. Balovich, C. G. Collins and J. Adriani.—p. 151.
On Learning Anesthesia. W. Bourne.—p. 157.
Effects of Premedication upon Signs of Asphyxia During Nitrous Oxide-Oxygen Anesthesia. C. R. Allen, R. S. Echols, K. C. O'Neal and H. C. Slocum.—p. 164.
*Therapeutic Uses of Intravenous Procaine. D. J. Graubard and M. C. Peterson.—p. 175.
Blood Transfusion Reactions: Their Etiology, Prevention and Treatment. S. J. Wilson.—p. 188.
Some Suggestions for Conduct of Continuous Spinal Anesthesia. W. E. Brown.—p. 193.
Use of Cell Suspensions to Determine Cytotoxicity of Local Anesthetics. L. A. Gittelson.—p. 202.
Effectiveness and Toxicity of Methadon, a New Analgesic Agent. R. C. Batterman and A. M. Oshlag.—p. 214.

Intravenous Procaine in Cardiac Disturbances During Anesthesia.—Burstein administered 100 mg. of procaine hydrochloride in 1 per cent solution to 4 patients, 2 men aged 27 and 40 years, respectively, and 2 women aged 43 and 69, respectively, for combating cardiac disturbances during general anesthesia for pericardiectomy, thyroidectomy and inguinal hernioplasty.

Procaine, a local anesthetic drug but a central nervous system stimulant, tends to diminish the cardiac hyperirritability produced by general anesthetic agents. It rendered an irregular pulse regular in 2 patients, diminished tachycardia and hypertension to normal limits in 1, and returned bradycardia and hypotension to normal limits in 1. But it is no cure-all and has its limitations. Six reports from other clinics substantiate the observations of the author. Two patients recovered from ventricular fibrillation following the intravenous injection of procaine hydrochloride. Intravenous use of procaine hydrochloride is also recommended as a prophylactic measure to minimize cardiac disturbances during general anesthesia. Results in 2 men who were aged 60 and 68 showed that with this technic cyclopropane may be administered to patients with preexisting cardiac disease without the manifestation of any apparent deleterious cardiovascular effects. Instantaneous recording electrocardiography is suggested as a helpful addition to the armamentarium of the anesthesiologist. The importance of proper diagnosis of cardiac arrhythmias is stressed.

Therapeutic Uses of Intravenous Procaine.—Graubard and Peterson employed intravenous administration of procaine hydrochloride as a safe hospital procedure under controlled conditions in a series of 448 cases in which 1,954 infusions of the drug were given in one year without morbidity or mortality. There were 224 patients with traumatic conditions, including 31 with fractures treated after reduction, 36 with low back pain due to myofascitis and 33 with reflex sympathetic dystrophy, in whom the results obtained with the drug in the management of pains were uniformly good. There were 194 patients with inflammatory conditions. Intravenous administration of procaine hydrochloride in conjunction with vitamin C provided persistently good results in arthritis, but the drug is still considered in the investigative stage. The improvement noted in patients with spastic conditions of neurologic origin recommends this form of treatment for further clinical study. Results with procaine hydrochloride seemed superior to those obtained with curare. Procaine hydrochloride is an adjuvant in the treatment of selected, traumatic, inflammatory and spastic conditions.

Annals of Internal Medicine, Lancaster, Pa.

30:495-712 (March) 1949

Q Fever—Review of Current Knowledge. R. J. Huebner, W. L. Jellison and M. Dorthy Beck.—p. 495.
*Clinical Aspects of Q Fever in Southern California; Study of 80 Hospitalized Cases. R. B. Denlinger.—p. 510.
Cough as Symptom of Cardiovascular Disease. J. H. Currens and P. D. White.—p. 528.
Prevention of Recurrences in Peptic Ulcer. T. L. Althausen.—p. 544.
Visceral Thrombophlebitis Migrans. I. S. Gerber and M. Mendlowitz.—p. 560.
*Conditioned Reflex Treatment of Chronic Alcoholism. X. Analysis of 3,125 Admissions Over a Period of Ten and a Half Years. W. L. Voegtlin and W. R. Broz.—p. 580.
*Liver Function and Serum Protein Structure in Gout. W. Q. Wolfson, C. Cohn, R. Levine and others.—p. 598.
Transient "O" Diastolic Blood Pressure (Indirect) in Upper Extremities. I. Stein.—p. 615.
Intermittent Dosage Schedules of Streptomycin with Resultant Prolonged Sensitivity of M. Tuberculosis. V. F. Deyke, M. W. Fisher, L. A. James and L. J. Sides.—p. 619.
Recent Advances in Study of Arteriosclerosis. S. O. Waife.—p. 635.

Clinical Aspects of Q Fever in California.—According to Denlinger, Q fever has been occurring in the general population of Southern California. Eighty hospitalized patients were selected for clinical study. Of this number, one third denied exposure to cattle or unpasteurized milk. Eighty per cent of the patients were adult males. The commonest symptom complex was that of a sudden onset of fever, sensations of chilliness, malaise, anorexia and severe headache followed in a few days by a slight hacking cough and mild pleuritic chest pain. The patients were febrile, had a relative bradycardia and appeared acutely ill. Localizing physical observations were indicative of pneumonia or meningism or were entirely lacking. The fever persisted from seven to fifteen days and subsided by lysis. Convalescence was usually rapid and complete but was occasionally prolonged. Two patients had mild relapses requiring their rehospitalization. The results of therapy with penicillin, sulfonamide compounds, roentgen radiation, streptomycin and para-aminobenzoic acid were inconclusive. Aureomycin was not used in the treatment of these patients. The blood counts were variable but commonly revealed a mild polymorphonuclear leukocytosis and lymphocytopenia. The erythrocyte sedimentation rate was elevated in every case. The spinal fluid was normal except for some increase in pressure and slightly decreased chloride content. Reactions to Proteus OX 19 and cold agglutination tests were negative. Roentgenograms of the chest showed infiltrations in the majority of cases, usually a uniform segmental or lobular consolidation. The complement fixation test for Q fever became positive during the second week of illness. The final diagnosis of Q fever was dependent on this test in every instance.

Conditioned Reflex Treatment for Chronic Alcoholism.—Voegtlin and Broz analyzed data concerning 3,125 patients admitted to the Shadel Sanitarium in Seattle for the treatment of chronic alcoholism. A series of 2,323 cases of treatment by the conditioned reflex has been subjected to statistical evaluation. Conditioning procedures, when used alone, will cause 85 per cent of chronic alcoholic patients to remain abstinent for six months or longer; 70 per cent will remain abstinent for one year or longer; 60 per cent will remain abstinent for two years or longer; 55 per cent will remain abstinent three years or longer; 40 per cent will remain abstinent four years or longer; over 30 per cent will remain abstinent for seven years or longer, and about 25 per cent will remain abstinent ten and a half years or longer. The value of conditioning therapy has been proved by these data. Adjuvant methods, such as psychotherapy, social service and rehabilitation, and physical rejuvenation should enhance the results when these measures are combined with conditioning methods, but this, as yet, has not been proved. The struggle against chronic alcoholism requires the use of every weapon of proved value. Conditioning technics should be thoroughly mastered and incorporated into existing therapeutic plans.

Liver Function and Serum Protein Structure in Gout.—Wolfson and co-workers studied serum protein partition to check tests which depend primarily on serum globulin structure and to aid in comparing changes in gout with those reported in rheumatoid arthritis. Forty-three patients were classified in four groups: (1) interval gout, (2) acute and subacute gouty arthritis, (3) chronic gouty arthritis and (4) gout with known complicating disease. They found that results of sensitive liver function tests indicate that gout is not uniformly associated with functional hepatic impairment. Diffuse disease of the liver can therefore be neither the cause of gout nor a uniform consequence of gout. Abnormal reactions to liver function tests are infrequent in uncomplicated interval gout. Most of the abnormalities are found to occur in patients with known complicating disease, and in these patients the degree of functional hepatic impairment is commensurate with the nature and severity of the associated disease. Diffuse hepatic involvement and alterations in circulating protein are not fundamental to the pathogenesis of gout.

Archives of Internal Medicine, Chicago

83:119-248 (Feb.) 1949

*Epidemiologic Aspects of Thyrotoxicosis. E. Meulengracht.—p. 119.
*Lymphosarcoma of Gastrointestinal Tract: Report of 21 Cases. M. A. Spellberg and S. Zivin.—p. 135.
Circulatory and Diuretic Effects of Theophylline Isopropanolamine. D. M. Fowell, J. A. Winslow, V. P. Sydenstricker and N. C. Wheeler.—p. 150.
Experimental Pulmonary Infarction: Abnormal Pulmonary Circulation as Prerequisite for Pulmonary Infarction Following an Embolus. D. W. Chapman, L. J. Gugle and P. W. Wheeler.—p. 158.
Acute Phosphorus Poisoning. H. J. Rubitsky and R. M. Myerson.—p. 164.
Infectious Mononucleosis with Neurologic Complications: Report of Fatal Case. V. B. Dolgopol and G. S. Husson.—p. 179.
Syphilis: Review of Recent Literature. H. A. Tucker, C. F. Mohr, R. D. Hahn and J. E. Moore.—p. 197.

Thyrotoxicosis.—Meulengracht states that during the years 1941 to 1945 there occurred a striking epidemic of thyrotoxicosis in Denmark. He reviews earlier observations on the epidemic occurrence of thyrotoxicosis. In Norway there was a genuine epidemic in the years 1941 to 1943. In France, but apparently confined to Paris, there was an epidemic in the years 1941 to 1944, with its peak in 1942 to 1943. The number

of patients admitted to the public hospitals in Paris rose to three or four times what it had been in the years immediately before. The author considers various factors that may cause a temporary rise in frequency and advances the hypothesis that a specific infective agent may be the cause of such epidemics.

Lymphosarcoma of Gastrointestinal Tract.—Spellberg and Zivin believe that lymphosarcoma of the gastrointestinal tract is of interest not only because of its rarity but because of the diagnostic difficulties and its difference in therapeutic response from other malignant lesions of the gastrointestinal tract. In 11 of the 21 cases reviewed by the authors the primary lesion was in the stomach; in the remaining 10 it was in the intestine. There are 88 cases of gastric carcinoma for each case of gastric lymphosarcoma. Roentgenologic examination usually fails to establish a diagnosis; gastroscopic examination may be of help. The prognosis of the small cell type of lymphosarcoma is better than that of the reticulum cell type. Resection followed by irradiation is the treatment of choice. The prognosis of gastric lymphosarcoma appears to be better than that of gastric carcinoma. Of the 10 cases of primary intestinal lymphosarcoma which were observed between 1931 and 1946, in 5 cases the lesions were located in the small intestine and in 5 in the large intestine. Three hundred colonic carcinomas were seen for each lymphosarcoma, which shows that this neoplasm is extremely rare in the colon. Intestinal lymphosarcoma appears to carry an extremely poor prognosis; no patient survived five years and most died in less than six months.

Archives of Neurology and Psychiatry, Chicago

61:99-226 (Feb.) 1949

Interpretation of Electromyogram. D. Denny-Brown.—p. 99.
Spasmodic Torticollis: I. Physiologic Analysis of Involuntary Motor Activity. E. Herz and P. F. A. Hoefer.—p. 129.
Chronic Rheumatic Encephalitis, Torsion Dystonia and Hallervorden-Spatz Disease. C. E. Benda.—p. 137.
Acid Phosphatase in Senile Brain. H. Josephy.—p. 164.
Efficacy of Brief Clinical Interview Method in Predicting Adjustments: Five Year Follow-Up Study of 304 Army Inductees. J. A. Aita.—p. 170.
Folie à Deux (Psychosis of Association). E. Ascher.—p. 177.
Optokinetic Response and Intracranial Lesions. D. G. Cogan and D. R. Loeb.—p. 183.
*Effects of Electroconvulsive Therapy on Diuretic Response to Water in Psychotic Patients. M. D. Altschule and K. J. Tillotson.—p. 188.
Tetraethylammonium Chloride in Treatment of Herpes Zoster and Intercostal Neuralgia. R. L. Fisher, M. Zukerman and D. J. Sweeny Jr.—p. 194.
Neurologic Manifestations Associated with Vitamin A Deficiency in Young Ducks: Clinical and Pathologic Study. D. E. Fletcher and R. H. Rigdon.—p. 199.

Electroconvulsive Therapy and Diuretic Response to Water.—Altschule and Tillotson say that earlier observations in their laboratory revealed that water retention occurs in association with the rapid gain in weight shown by patients who improve during the course of electroshock therapy. Stimulation of the posterior lobe of the pituitary consequent to hemoconcentration or to severe muscular effort, both of which occur during electrically induced convulsions, may cause liberation of antidiuretic hormones. The effect of steroid hormones is to cause salt and water retention. The action of these hormones is apparently increased during electroshock therapy. Since hormones of the posterior lobe of the pituitary inhibit water diuresis, a study of the diuretic response to water before and after electroshock therapy might help in the evaluation of the possible role of hormonal factors in causing the changes in water content of the tissues which result from this treatment. Sixteen patients ranging in age from 19 to 73 years were studied. Depressed patients who had not been treated or who were in relapse might show retarded diuresis after the ingestion of water, and patients with schizophrenic syndromes might exhibit abnormally accelerated and excessive diuretic responses. After electroconvulsive therapy the diuretic response to water was accelerated in all patients who gained weight as a result of treatment and was not accelerated in those whose weight was unchanged. It is concluded that the gain in weight previously shown to be associated with retention of water is not a consequence of increased activity of antidiuretic substances. It should not be concluded, however, that stimulation of the posterior lobe of the pituitary does not occur at all as a consequence of electroshock therapy. The data show only that if such stimulation of the posterior lobe does occur it is not sufficient to result in retardation of the diuretic response to water.

Archives of Otolaryngology, Chicago

49:125-242 (Feb.) 1949

*Abscess of Frontal Lobe Secondary to Ethmoiditis. J. H. Kler.—p. 125.
Surgery of the Chronically Discharging Ear. H. P. House.—p. 135.
*Ménière's Syndrome: Observations on Vitamin Deficiency as Causative Factor; I. Vestibular Disturbance. M. Atkinson.—p. 151.
Esophageal Varices in Banti's Disease: Report of Two Cases in Which Condition Was Improved with Injection of Sclerosing Solutions. R. B. Lewy.—p. 175.
Otosclerosis Associated with Osteoporosis and Labyrinthitis Chronica Ossificans. H. Brunner.—p. 184.
Unusual Otitic Foreign Bodies: Report of Two Cases. W. C. Warren Jr. and T. E. Bivins.—p. 196.
pH of Cutaneous Surface of External Auditory Canal: Study of Twenty-Seven Infants, Forty-Four Children and Sixty Adults. N. D. Fabricant and M. A. Perlstein.—p. 201.
Progress in Surgery of Septum. R. Kayser.—p. 210.

Abscess of Frontal Lobe and Ethmoiditis.—Kler reports 1 case of acute abscess of the frontal lobe resulting from an infection of the upper respiratory tract followed by ethmoidal empyema and periorbital abscess in a child aged 5, and 2 cases of chronic abscess of the frontal lobe resulting from a low grade chronic ethmoiditis of many years' duration in 2 men. The brain abscess in the first case was the result of an acute and virulent infection to which the patient had not been able to develop an adequate resistance. It is found, as a rule, as a complication of acute ethmoiditis. Chronic infection in the ethmoid sinuses, as in the 2 other cases, is the principal cause of brain abscess of ethmoid origin. The extension of the infection is by contiguity, either by osteitis, causing local necrosis with subsequent local meningitis, encephalitis and formation of subcortical abscess, or by thrombophlebitis of any of the veins communicating with the dura. Complications of acute ethmoiditis are more frequent and more easily diagnosed than those of the chronic infection. Chronic abscess of the brain as a complication of chronic ethmoiditis is an encapsulated abscess that gives few general or localizing signs. Papilledema was the most constant observation. Headache is a late symptom, and one that should be regarded as a danger signal. Electroencephalography is an invaluable aid in the diagnosis of this type of intracranial complication. The assistance of the neurosurgeon in the management of these cases is essential.

Ménière's Syndrome.—Atkinson studied 87 patients between the ages of 23 and 62, who had Ménière's syndrome with the triad of acute paroxysmal vertigo, deafness and tinnitus, from the standpoint of deficiency in the three major components of the vitamin B complex, nicotinic acid, riboflavin and thiamine. The responses of the patients to a standard dose of histamine diphosphate administered intradermally were recorded; the types of vertigo of which the patients complained were noted and a chart was kept of the symptoms generally accepted as accompanying certain vitamin deficiencies. Results showed that patients with Ménière's syndrome experience two distinct types of vertigo, rotational and positional, which are associated with different and specific vitamin deficiencies. Twenty patients who experienced rotational vertigo alone showed signs of nicotinic acid deficiency in the tongue, gave a small response to histamine and were relieved of their attacks with nicotinic acid. Twenty-four patients experienced positional vertigo alone, showed signs of riboflavin deficiency in the tongue, the eyes and the skin, gave a large response to histamine and were relieved of their attacks with riboflavin. Forty-three patients, the majority, experienced both kinds of vertigo and showed signs of deficiency of two fractions of the vitamin. They gave an intermediate response to histamine and were relieved of their attacks only if the two fractions were administered. Other symptoms common in patients with Ménière's syndrome can be related to other deficiencies; the fatigue, irritability and palpitations associated with thiamine deficiency may be relieved by administration of the appropriate vitamin. The therapeutic doses of the vitamins were considerably larger than those usually advocated. The full dose must be arrived at gradually, starting with small doses given parenterally and orally and increasing the doses slowly until the attacks are controlled.

Archives of Pathology, Chicago

46:401-502 (Nov.) 1948

Aging Processes in Ovaries of Mice Belonging to Strains Differing in Incidence of Mammary Carcinoma. L. Loeb.—p. 401.
Effects of Folic Acid Antagonists Inoculated in Embryonate Eggs. P. F. Wagley and H. R. Morgan.—p. 441.
Cholesterol of Human Adrenal Gland: Its Significance in Relation to Adrenal Function and Structure. W. F. Rogers Jr. and R. H. Williams.—p. 451.
Reticulum Cell Sarcoma of Bone. V. R. Khanolkar.—p. 467.
Neoplastic Diseases of Dogs: II. Mast Cell Sarcoma, Lymphosarcoma, Histiocytoma. R. M. Mulligna.—p. 477.
Fatal Viral Hepatitis Complicated by Phlegmonous Cecitis and Ileocecal Intussusception. W. Umiker.—p. 493.
Method for Biopsy of Bone Marrow of Experimental Animals. H. B. Ritter and J. J. Oleson.—p. 498.

Bulletin of Johns Hopkins Hospital, Baltimore

84:285-408 (April) 1949

Relation of Potassium to Neurologic Manifestations of Hypocalcemic Tetany. F. L. Engel, S. P. Martin and H. Taylor.—p. 285.
Investigation into Presence of Antibodies and Hypersensitivity in Encephalitis Produced Experimentally by Injection of Homologous Brain Suspensions. K. R. Hill.—p. 302.
Anti-Pneumococcal Powers of Blood in Alloxan Diabetes in Rabbit. A. H. Cruickshank and T. P. B. Payne.—p. 334.
Effect of Exercise on Renal Mechanism of Electrolyte Excretion in Normal Subjects. A. A. Kattus, B. Sinclair-Smith, J. Genest and E. V. Newman.—p. 344.
Renal Mechanism of Electrolyte Excretion and Metabolic Balances of Electrolytes and Nitrogen in Congestive Cardiac Failure; Effects of Exercise, Rest and Aminophyllin. B. Sinclair-Smith, A. A. Kattus, J. Genest and E. V. Newman.—p. 369.

Cancer Research, Baltimore

9:193-256 (April) 1949. **Partial Index**

Adrenal Medullary Tumors (Pheochromocytomas) in Mice. F. W. Smith, W. U. Gardner, Min Hsin Li and H. Kaplan.—p. 193.
Histopathologic Study of Mode of Inhibition of Cellular Proliferation by Urethane: Effect of Urethane on Walker Rat Carcinoma 256. J. W. Green Jr. and C. C. Lushbaugh.—p. 199.
Preparation and Properties of Mitochondria and Submicroscopic Particles of Normal and Leukemic Mouse Organs. R. B. Alfin-Slater, A. M. Larack and M. L. Petermann.—p. 215.
Effect of Walker Carcinoma 256 on Total Lipid Content of Rats. G. B. Mider, C. D. Sherman Jr. and J. J. Morton.—p. 222.
Volume of Cell Nuclei in Amputation Neuromas and in Neurofibromas. R. Altschul and A. M. Friesen.—p. 225.
Intratracheal Transplantation with Brown-Pearce Carcinoma. T. T. Bronk and M. Appel.—p. 228.
Tissue Culture Experiments on Biologic Action of Methyl bis (Beta-Chlorethyl) Amine and Its Hydrolysis Products. H. B. Fell and C. B. Allsopp.—p. 238.
*Nodular Hyperplasia of Thyroid Glands Induced by Thiouracil. G. L. Laqueur.—p. 247.

Nodular Hyperplasia of Thyroid Induced by Thiouracil.—Laqueur describes studies on male and female albino rats. There were changes in weight and morphology of the thyroid and hypophysis following prolonged administration of thiouracil. A progressive increase in weight of the two organs was limited to the female rats. There was evidence of involution of the thyroid in male rats which had received the diet for ten months. The regressive changes in the thyroid were associated with cytologic alterations in the hypophyses. Diffuse hyperplasia of the thyroid was the most uniform response to the drug. Definite nodular hyperplasia was found in 33 per cent of all the rats. The histologic structure of the nodules varied, and the same gland harbored nodules of different histologic appearance in several instances. The anterior pituitary thyrotropic hormone is responsible for the hyperplastic changes in the thyroid after administration of antithyroid compounds, because hyperplasia is abolished in the hypophysectomized animal. Observations indicate that the thyrotropic hormone reaches the thyroid long enough and in such a quantity that active thyroid hyperplasia persists. Diffuse hyperplasia is the earliest and most uniform response to antithyroid agents. Nodular hyperplasia may develop later. The observations on mice in which nodules do not develop in the thyroid gland after prolonged exposure to these agents are of importance. It seems reasonable that the cause for the development of nodules should be looked for in the thyroid itself. Since spontaneous tumors in that gland are rare in young rats, it may be suggested that the activity of the pituitary thyrotropic hormone provides the growth stimulus and that the formation of nodules is one of the responses of which the thyroid is capable.

Connecticut State Medical Journal, Hartford

13:287-408 (April)1949

Some Modern Aspects of Lymphomas and Leukemias. L. F. Craver.—p. 302.
What General Practitioners Should Know About Dermatology. G. C. Andrews.—p. 309.
Diagnosis of Disease Arising from Occupation: Some Special Features and Pitfalls. L. C. McGee.—p. 315.
Orbital Tumors: Reports of Cyst of Inferior Oblique Tendon: Other Rare Orbital Tumors: Review of Literature. H. L. Birge.—p. 319.
Intussusception Associated with Small Bowel Tumors. R. M. Lowman, L. L. Waters and W. Mendelsohn.—p. 327.
Despotism by Consent of Governed. J. H. Howard.—p. 333.

Endocrinology, Springfield, Ill.

44:293-390 (April) 1949. **Partial Index**

Quantitative Studies of Cell Types in Rat Hypophysis Following Unilateral Adrenalectomy. J. C. Finerty and B. Briseno-Castrejon.—p. 293.
Effect of Hypnotics on Blood Sugar and Action of Insulin. E. Larson.—p. 301.
Hydrolysis of Conjugated Sulfates of Estrogens by Commercial Enzyme Preparation of Aspergillus Oryzae. H. Cohen and R. W. Bates.—p. 317.
Preliminary Observations on Antidiuretic Substance Recovered from Urine of Patients with Cirrhosis of Liver. G. H. Stueck Jr., S. H. Leslie and Elaine P. Ralli.—p. 325.
Involution of Adrenal Cortex of Rats Treated with Thiouracil. M. X. Zarrow and W. L. Money.—p. 345.
Influence of Steroid Hormones on Granulation Tissue. M. Taubenhaus and G. D. Amromin.—p. 359.
Quantitative Relation Between Certain Amino Acids and Glycogenesis as Influenced by Adrenalectomy and Adrenal Replacement. J. Awapara, H. N. Marvin and B. B. Wells.—p. 378.

Hawaii Medical Journal, Honolulu

8:251-320 (March-April) 1949

Studies on Cultivation of Leprosy Bacillus. K. Nakamura.—p. 265.
Maternal Mortality in Hawaii. Janet M. Boog.—p. 267.
Epidemic Keratoconjunctivitis. W. J. Homes.—p. 272.
Pneumatosis Cystoides Intestini: Causing Obstruction of Small Intestine. M. Gerundo and M. L. Chang.—p. 273.
Intravenous Procaine: New Uses for Old Drug. J. S. Horan.—p. 276.

Industrial Medicine, Chicago

18:133-176 (April) 1949

Cornell Index Used as Appraisal of Personality by Industrial Health Service—I. Total Score. J. S. Felton.—p. 133.
A 500-Employee Medical Department Layout. C. E. Martin.—p. 145.
Health is Big Business for Small Industries. J. J. Wittmer.—p. 146.
College Course on Medical Basis of Accident Compensation—As Taught at Swiss Universities. F. Zollinger.—p. 149.
*Ptomaine Food-Poisoning a Myth. G. M. Dack.—p. 151.
Surgery of Gastric Ulcer. W. Walters.—p. 155.
*Industrial Accidents and Peripheral Vascular Diseases. S. S. Samuels.—p. 157.
New Approach to Problem of Impaired Health. W. R. P. Emerson.—p. 159.
Ambulatory Treatment of Leg Ulcers with Pressure Bandages. O. Meyer.—p. 161.
Problems in Control of Occupational Cancer. W. C. Hueper.—p. 163.
Medical Testimony. L. R. Ellars and W. M. Twyman.—p. 167.

Ptomaine Food-Poisoning a Myth.—Dack points out that the term ptomaine poisoning was coined in 1870 and was associated in those times with putrefaction, particularly alkaline extracts of protein decomposition. The commonly recognized chemical poisons, arsenic, copper, antimony and lead, were early ruled out as the causal factor of ptomaine poisoning. Later, while bacterial toxins, particularly those of the Salmonella group and of Bacillus botulinus were searched for in cases of food poisoning, a bacterium as omnipresent and as common as the staphylococcus was completely ignored. The author describes his studies on a hemolytic staphylococcus that was isolated in a case of food poisoning. He is convinced that this is the most frequent type of food poisoning and cites some of the large outbreaks that occurred during the last war. The best control is adequate refrigeration. If foods are adequately refrigerated, then the staphylococcus does not grow and produce its poison. Some strains of staphylococci do not produce this poison. It is not known how many of them do. Complete studies have not been made. This type of food poisoning has been most commonly spoken of as ptomaine food-poisoning.

Industrial Accidents and Peripheral Vascular Disease.—Samuels calls attention to the close relation between peripheral vascular diseases and serious complications resulting from slight trauma. Many cases of leg amputations for gangrene have

resulted in delayed claims for compensation. After the leg has been removed the patient may recall that the gangrene preceding the amputation was produced by some insignificant trauma. Patients with preexisting arterial insufficiency in the extremities, as in Buerger's disease or arteriosclerosis obliterans, are particularly susceptible to the development of gangrene if subjected to minimal trauma which would not be serious if the circulation were normal. The patient with preexisting arterial insufficiency in the extremities is susceptible to effects of exposure to a cold environment to a much greater degree than a person with normal circulation. Workers in butcher shops or refrigerated food compartments, as in ship storage rooms, or employees in street-cleaning departments are all candidates for the disability if the circulation in the extremities is deficient. The increasing use of electrical vibrating tools and pneumatic hammers has produced a form of Raynaud's syndrome of the fingers and hands which may cause total disability. Evidence of this condition indicates the advisability of immediate change of occupation. Many prospective employees with advanced arterial disease of the lower extremities slip through physical examination undetected in occupations where such a disease would be a serious hazard. Physicians have not been sufficiently trained in the detection of arterial disturbance. A simple test consists in having the patient, while in a recumbent position, elevate the legs to an angle of about 45 degrees. The feet are then flexed and extended rapidly at the ankle joints, and the plantar surfaces are observed. If ischemia should develop, this is evidence of organic arterial insufficiency.

Journal of Bacteriology, Baltimore

57:269-388 (March) 1949. **Partial Index**

Serologic Study of Members of Pseudomonas Genus. J. Munoz, M. Scherago and R. H. Weaver.—p. 269.

*Effect of Ultrasonic Waves upon Klebsiella Pneumoniae, Saccharomyces Cerevisiae, Miyagawanella Felis, and Influenza Virus. A. D. Hamre. —p. 279.

Demonstration of Viral Inclusion Bodies in Unstained Tissue Sections with Aid of Phase Microscope: I. Inclusion Bodies of Yellow Fever, Herpes Simplex, Fowl Pox, and Distemper. J. J. Angulo, O. W. Richards and A. L. Roque.—p. 297.

Circulin, Antibiotic from Organism Resembling Bacillus Circulans. F. J. Murray and others.—p. 305.

Some Remarks on Image Contrast in Electron Microscopy and Two-Component Objective. J. Hillier.—p. 313.

Internal Structure and Nuclei in Cells of Escherichia Coli as Shown by Improved Electron Microscopic Techniques. J. Hillier, S. Mudd and A. G. Smith.—p. 319.

Fungus-Inhibitive Properties of Bromoacetamides. J. M. Leonard and V. L. Blackford.—p. 339.

Chloramphenicol (Chloromycetin) in Experimental Cholera Infections. R. L. Gauld and others.—p. 349.

Recovery from Ultraviolet Irradiation in Escherichia Coli. R. B. Roberts and E. Aldous.—p. 363.

Effect of Ultrasonic Waves.—Hamre states that two types of high frequency sound generators have been used: the magnetostriction oscillator, which produces vibrations at about 9,000 cycles per second, and the quartz crystal generator, in which the frequency of the sound depends on the crystal and can be as high as 800,000 cycles per second. In ultrasonic experiments with a quartz crystal generator the following factors must be taken into consideration: (1) the size of the crystal, (2) the frequency of the crystal, (3) the amplitude or intensity of the wave, (4) the distance between the top of the crystal and the bottom of the container used for the material to be treated, (5) the type of container used for the material to be treated, (6) the depth of liquid being treated, (7) the composition of the suspending medium for the cells being treated and (8) the type of cooling system used. She found that the mortality rate of Klebsiella pneumoniae was higher when the cell suspension was treated in a cellophane-bottomed container than when a glass container was used. The volume of liquid being treated was important. A decrease in the amplitude of the ultrasonic waves resulted in a decrease in the mortality of K. pneumoniae. A higher mortality rate of K. pneumoniae was obtained when the cells were suspended in broth than in 0.85 per cent sodium chloride or in buffer solution. However when 0.002 per cent sorbitan monooleate was added to the saline solution to give the same surface tension as broth, the mortality rate of K. pneumoniae was the same as it was in broth suspensions. The mortality rate of Saccharomyces cerevisiae was about the same in broth suspensions and in buffer suspensions. Electron micrographs of K. pneumoniae and Flavobacterium cerevisiae showed the ruptured cells and cell walls. Miyagawanella felis (the agent of feline pneumonitis) was inactivated by ultrasonic energy after twenty minutes' treatment. An increase in the amount of agent was observed after ten minutes' treatment, probably due to the dispersion of aggregates of the elementary bodies. Ultrasonic energy also inactivated influenza virus A (PR8 strain). In none of the ultrasonic experiments conducted was 100 per cent of the cells or virus destroyed.

Journal of Immunology, Baltimore

61:209-282 (March) 1949

Studies in Dysentery Vaccination: VI. Primary Vaccination of Children with Polyvalent Vaccines of Shigella. M. L. Cooper, J. Tepper and H. M. Keller.—p. 209.

Id.: VII. Response of Children to Booster Injections of Shigella Vaccines. M. L. Cooper, J. Tepper and H. M. Keller.—p. 221.

Immune Response in Mice After Vaccination with Bacterium Tularense. I. Ruchman and L. Foshay.—p. 229.

Evaluation of Test for Antihemagglutinin in Diagnosis of Infections by Mumps Virus. F. C. Robbins, L. Kilham, J. H. Levens and J. F. Enders.—p. 235.

Specificity of Agglutination-Reaction with Autoclaved Hemolytic Streptococci and Role of Group-Specific Polysaccharide in Reaction. S. J. Liao.—p. 243.

Precipitin Production in Chickens: IV. Comparison of Antibody Responses of Eight Avian Species. H. R. Wolfe and E. Dilks.—p. 251.

Studies in Metabolism of Tubercle Bacillus: I. Production of Riboflavin. M. I. Smith and E. W. Emmart.—p. 259.

Relation of Shigella Type-Specificity and Susceptibility to Antibiotic-Producing Strains of Escherichia Coli. S. P. Halbert and M. Gravatt. —p. 271.

Journal of Investigative Dermatology, Baltimore

12:145-202 (March) 1949. **Partial Index**

Histadyl Cream in Treatment of Pruritic Dermatoses. S. Epstein and W. L. Macaulay.—p. 145.

Serum Concentration Following Oral Administration of Crystalline Procaine Penicillin G and Crystalline Sodium Penicillin G. D. K. Kitchen, E. W. Thomas and C. R. Rein.—p. 147.

Dermatitis Due to Antihistaminic Agents. E. Epstein.—p. 151.

Treatment of Herpes Zoster with Moccasin Venom. C. C. Dennie, D. B. Morgan and F. P. Coombs.—p. 153.

Effects Produced on Pilosebaceous System and Adrenals of Rabbit by Inunction of Sex Hormones. F. Reiss and S. Gellis.—p. 159.

Failure of Fatty Acid Salts to Lessen Cutaneous Irritation Caused by Adhesive Plaster. L. E. Gaul and G. B. Underwood.—p. 173.

Immediate Wheal and 24-48 Hour Tuberculin Type Edematous Reactions to Trichophytin. O. F. Jillson and M. Huppert.—p. 179.

Weight of Skin. M. Leider.—p. 187.

Journal of Lab. and Clinical Medicine, St. Louis

34:439-586 (April) 1949. **Partial Index**

*Response of Lingual Manifestations of Pernicious Anemia to Pteroylglutamic Acid and Vitamin B_{12}. J. F. Schieve and R. W. Rundles. —p. 439.

Capillary Fragility Studies (Göthlin Test) on One Hundred Patients Receiving Dicumarol. R. A. Jubelirer and H. I. Glueck.—p. 448.

Use of Russell Viper Venom and Lecithin as Thromboplastin in Estimation of Prothrombin. C. A. Mawson.—p. 458.

Protamine Titration as Indication of Clotting Defect in Certain Hemorrhagic States. J. G. Allen and others.—p. 473.

Enzyme Studies on Human Blood. III. Effect of Plasma Proteins on Coagulation. G. Y. Shinowara.—p. 477.

Use of Urinary Pigment Excretion for Measurement of Basal Metabolic Rate. J. J. Vorzimer, I. B. Cohen and J. Joskow.—p. 482.

Exacerbation of Alloxan Diabetes in Mice by Injection of Typhoid Vaccine: Role of Adrenal Gland. L. Tobian Jr. and W. L. J. Edward. —p. 487.

Excretion of Penicillin in Human Milk. R. Rozansky and A. Brzezinsky. —p. 497.

Bacterimetric Studies III. Blood Level Studies on Teropterin Metabolism. G. Toennies and D. L. Gallant.—p. 501.

Study of Some Factors Involved in Colorimetric Determination of Caronamide. H. S. Collins and M. Finland.—p. 509.

Dimethylether of d-Tubocurarine Iodide. E. E. Swanson, F. G. Henderson and K. K. Chen.—p. 516.

Hereditary Angioneurotic Edema, with Case Report. J. M. Sheldon, E. O. Schreiber and R. G. Lovell.—p. 524.

Occurrence of False Positive Trichina Precipitin Tests in Infectious Mononucleosis. F. A. Bassen, A. E. Thomson and A. Silver.—p. 543.

Chronic Typhoid Carrier: II. Effect of Cholecystectomy on Bacteriologic Course. A. Littman, J. A. Vaichulis and A. C. Ivy.—p. 549.

Lingual Manifestations of Pernicious Anemia.—Schieve and Rundles treated 8 patients with atrophy and inflammation of the lingual mucosa, resulting from pernicious anemia with pteroylglutamic acid. During the first month patients were given 75 to 100 mg. of the drug by mouth and for the next two months 30 to 50 mg. daily. In 2 of these patients treat-

ment with pteroylglutamic acid produced a rapid restoration of normal lingual mucosa. The tongue remained normal, and there was neurologic improvement, in spite of an incomplete hematologic remission. In 4 other patients pteroylglutamic acid failed to produce an adequate lingual response. Liver extract was more effective in correcting the lingual and other manifestations of the disease. The last 2 patients treated with pteroylglutamic acid had distinct lingual relapses during the third month of treatment, in spite of satisfactory hematologic and neurologic responses. The lingual abnormalities disappeared within five to seven days after the injection of vitamin B_{12}. In 5 patients showing the lingual manifestations of untreated pernicious anemia the injection of vitamin B_{12} in a dose of 0.001 mg. daily to 0.010 mg. in a single dose led to regeneration of lingual papillae in five to seven days. Results suggest that treatment with pteroylglutamic acid has an irregular effect on all manifestations of the pernicious anemia rather than failing consistently in anyone. The cause for individual variability in therapeutic response remains to be determined.

Journal-Lancet, Minneapolis

69:119-152 (April) 1949

General Practitioner's Part in Eradication of Tuberculosis. S. A. Slater. —p. 120.
Active Pulmonary Tuberculosis Following Negative 70 mm. Film Impressions in Minneapolis Mass Chest X-Ray Survey. W. Roemmich. —p. 122.
Tuberculosis Control in Colleges. M. L. Durfee.—p. 124.
Medical Students and Tuberculosis. C. H. Schmidt.—p. 128.
Immunobiologic Versus Exposition Prophylaxis of Disease in Medical Students, Particularly Tuberculosis. K. F. Meyer.—p. 129.
Fungus Diseases of Lungs. H. E. Miller.—p. 136.
Pneumonotomy with Open Drainage of Tuberculous Pulmonary Cavities (Cavernostomy). J. V. Thompson.—p. 141.
Tuberculous Osteomyelitis of First Rib Resulting in Brachial Plexus Compression: Case Report. E. H. Winterhoff and J. D. Murphy. p. 145.

Journal of the Mount Sinai Hospital, New York

15:337-392 (March-April) 1949

Functional Significance of Various Leukocytes in Inflammation. W. E. Ehrich.—p. 337.
Acute Renal Insufficiency Following Transfusion: Pathogenesis and Treatment. I. G. Kroop, A. P. Fishman, H. E. Leiter and A. Hyman. —p. 343.
Psychologic Study of Neurodermatitis with Case Report. E. D. Joseph, S. M. Peck and M. R. Kaufman.—p. 360.
Sarcosporidiosis in 2 Cases with Trichinosis. H. S. Arai.—p. 367.
Phrenic Nerve Paralysis Associated with Erb's Palsy in Newborn: Clinical and Anatomicopathologic Study. L. B. Turner and A. A. Bakst.—p. 374.
Hematoma of Rectus Abdominis Muscle Simulating Gynecologic Disease. R. I. Walter and R. Landesman.—p. 380.
Osteogenesis Produced by Chemical Extract of Bone. J. Hartley, S. S. Tanz and M. Schneider.—p. 383.

Journal National Malaria Society, Columbia, S. C.

8:1-114 (March) 1949. **Partial Index**

Physiologic Studies in Human Malarial Host: I. Blood Plasma, "Extracellular" Fluid Volumes and Ionic Balance in Therapeutic P. Vivax and P. Falciparum Infections. R. R. Overman, T. S. Hill and Y. T. Wong.—p. 14.
Summary of Experimental Use of DDT as Mosquito Larvicide. F. F. Ferguson, W. M. Upholt and S. W. Simmons.—p. 32.
Adrenal Hypertrophy in Chicks Infected with Plasmodium Gallinaceum. E. M. Nadel, D. J. Taylor, J. Greenberg and E. S. Josephson.—p. 70.
Hypersensitivity to Sulfadiazine of Chlorguanide-Resistant Strain of Plasmodium Gallinaceum. J. Greenberg.—p. 80.

J. Neuropathology & Exper. Neurology, Baltimore

8:125-254 (April) 1949. **Partial Index**

Herpes Simplex Encephalitis in Man, with Report of 3 Cases. W. Haymaker.—p. 132.
Spontaneous Ventricular Rhinorrhea and Otorrhea. A. E. Walker. —p. 171.
Pathology and Pathogenesis of Infectious Polyneuritis (Guillain-Barré Syndrome). I. M. Scheinker.—p. 184.
Experimental Hydrocephalus and Obliteration of Ventricles. L. Bakay Jr. —p. 194.
Cerebral Endarteritis Obliterans in an Infant. R. Altschul.—p. 204.
Lipoidosis of the Brain, Combined with Glycogenosis of the Liver. H. Josephy.—p. 214.
Cerebral Schistosomiasis. R. C. Bassett and K. Lowenberg.—p. 220.
Astroblastoma and Perithelial Sarcoma in a Case of Neoplastic Disease of the Brain. J. D. French.—p. 232.
Development Anomaly with Reduction of Lateral Horns of Spinal Cord in a Case of Congenital Megacolon (Hirschsprung's Disease). E. C. Alvord Jr., L. D. Stevenson and S. W. Dooley.—p. 240.

Journal of Thoracic Surgery, St. Louis

18:137-278 (April) 1949

*Malignant Nature of Bronchial Adenoma. A. Goldman.—p. 137.
Adenoma of Bronchus. C. B. Rabin and H. Neuhof.—p. 149.
Clinical Use of Prosthesis to Prevent Overdistention of Remaining Lung Following Pneumonectomy. J. Johnson, C. K. Kirby, C. S. Lazatin and J. A. Cocke.—p. 164.
Evaluation of Extrapleural Pneumonolysis with Lucite Plombage: Report of 51 Cases. J. C. Trent, J. D. Moody and J. S. Hiatt Jr.—p. 173.
Experimental and Clinical Study of Collapse Therapy Using Fiberglas Wool and Fabric. T. J. E. O'Neill, H. P. Redondo Ramirez and R. G. Trout.—p. 181.
Analysis of Variations of Segmental Bronchi of Right Lower Lobe of Fifty Injected Lungs. F. R. Smith and E. A. Boyden.—p. 195.
Analysis of Variations of Segmental Bronchi of Left Lower Lobe of Fifty Dissected, and Ten Injected, Lungs. R. M. Berg, E. A. Boyden and F. R. Smith.—p. 216.
*Alveolar Cell Carcinoma of Lung (Pulmonary Adenomatosis, Jagziekte?): Multicentric Tumor of Epithelial Origin. N. C. Delarue and E. A. Graham.—p. 237.
Ectopia Bronchi. W. H. Falor and A. H. Kyriadkides.—p. 252.
Lung Hernia: Case Report and Review of Literature. J. J. Hurwich. —p. 261.
Immediate Cardiovascular and Respiratory Adjustments to Pneumonectomy. J. H. Long, M. R. Wester and M. J. Oppenheimer.—p. 269.

Malignant Nature of Bronchial Adenoma.—Goldman reports 5 patients, 3 men and 2 women between the ages of 25 and 60, with bronchial adenoma showing malignant qualities. The most malignant changes were observed in the mixed tumor type of bronchial adenomas; in 1 case the complete transformation to a clinical and histologic picture of bronchiogenic carcinoma was observed, suggesting that carcinoma of bronchiogenic type may occasionally arise in a mixed tumor type of bronchial adenoma. Carcinoid types of bronchial adenoma not infrequently show metasatic involvement of the mediastinal lymph nodes; this occurred in 1 case in which the tumor was present for thirty years and in another in which the duration of symptoms was only a few months. Bronchial adenomas of carcinoid type occurred together with multiple tumors of low grade malignancy in other organs of 2 patients, suggesting that the stimulus for the production of bronchial adenoma is the same as that capable of producing neoplasms in other organs than the lung. The failure of bronchial adenoma to produce vascular seedings in 1 case, even though tumor cells were demonstrated floating in the lumen of a large pulmonary vein, suggests that the only favorable soil for bronchial adenoma is in the bronchi and lung. Lobectomy was performed in 2 of the author's cases and pneumonectomy in 1, giving approximately 100 per cent five year cures where this period of time had elapsed since operation. From the observation of tumors of over thirty years' duration, it would appear that several decades will be necessary to observe patients treated by lobectomy and pneumonectomy before the recurrence rate can be definitely established.

Alveolar Cell Carcinoma of Lung.—Delarue and Graham report 1 case of carcinoma of the lung in a man aged 35, which seems to have arisen in the cells lining the alveoli rather than in a bronchus. The preponderance of evidence allows one to consider this particular malignant pulmonary lesion, which is characterized by a reproduction of the alveolar structure of the lungs and the typically multiple arrangement of neoplastic areas, coupled with the failure to demonstrate a hidden primary tumor, as multicentric in origin and derived from endodermal elements. Consequently it is permissible to encourage the use of the term "alveolar cell carcinoma," implying the presence of epithelial cells lining the alveoli, malignant changes which are responsible for the production of a tumor such as presented by the author's patient. The case is illustrative and typical, demonstrating the slow growth of the neoplasm. The known duration of the patient's disease was at least six years. Initial lobectomy performed in 1943 resulted in freedom from symptoms for four years. In 1947 the remaining portion of the right lung was resected, since manifestations of the disease reappeared in this part of the lung. The microscopic pattern of the tumor observed at the second operation was similar to that seen at the first operation; there was evidence of local invasion of the chest wall. The regional lymph nodes were not involved. The patient was given intensive postoperative irradiation therapy, and when he was last seen, nine months after the second operation, bron-

choscopic observations were normal and there were no tumor cells observed in the smears from the bronchus. Surgical treatment has resulted in worth while palliation. Attention is called to the similarity of the disease in this case to jagziekte, the supposedly virus disease of South African sheep.

Medical Annals of District of Columbia, Washington

18:113-170 (March) 1949

Effect of Tetraethylammonium Chloride on Peripheral Blood Flow. J. R. Veal, J. N. Shadid and W. L. Jamison.—p. 113.
Surgical Aspects of Subarachnoid Hemorrhage. J. P. Murphy.—p. 119.
Jaundice in Myocardial Infarction. I. B. Brick.—p. 129.
Salmonella Choleraesuis Bacteremia Treated with Streptomycin: Report of Case. J. Selby and J. Tidler.—p. 134.
Scirrhous Carcinoma of Breast: Report of Case. S. T. Kimble.—p. 136.

18:171-228 (April) 1949

*Physiologic Basis for Treatment of Diabetic Coma. J. F. Fazekas and A. E. Parrish.—p. 171.
Vomiting Associated with Pregnancy. L. V. Dill.—p. 178.
Chronic Myelogenous Leukemia Treated with Urethane: Report of Case. W. D. Claudy.—p. 185.
Silas Weir Mitchell and the Tired Nerves. E. Podolsky.—p. 188.

Diabetic Coma.—According to Fazekas and Parrish, the brain depends on the circulating blood glucose as its principal source of energy. In so far as the cerebral tissues are concerned, insulin is not a necessary catalyst for the oxidation of glucose. In diabetic coma there is nevertheless a reduction of the cerebral cells to utilize the available glucose. The cerebral hypoxia is of the histotoxic type, and the acidosis and ketosis may be etiologic factors. Recovery from diabetic coma seems to be more closely correlated with the degree and duration of the depression of the cerebral metabolic rate than with the other biochemical alterations. In view of the sensitivity of the cerebral cells to anoxia, the administration of large doses of insulin is indicated as soon as the diagnosis is established, since it is most important to restore the cerebral metabolic rate to normal as rapidly as possible. Hypoglycemia should be avoided because of its depressant effects on cerebral metabolism. This is best accomplished by the administration of dextrose as soon as insulin activity becomes manifest and should be continued for at least six hours after the administration of the last large dose of insulin.

Military Surgeon, Washington, D. C.

104:247-330 (April) 1949. **Partial Index**

Military Responsibility for Civilian Health in War. R. W. Bliss.—p. 247.
Medical Field Service. J. I. Martin.—p. 250.
Regional Enteritis. R. M. Hardaway.—p. 259.
Spinal Cord Symptoms and Signs as First Manifestations of Cerebellar Medulloblastoma. S. W. Tuthill.—p. 264.
Carcinoma of Male Breast. G. Q. Lee.—p. 270.
Q Fever a Problem to Milk Industry. A. B. Rich and D. S. Robertson.—p. 276.
Psychotic States: Correlations of Biochemical and Histologic Changes in the Brain. R. de Rohan Barondes, R. H. Kuhns, D. I. Levine and C. E. Strachan.—p. 278.
New Diluent for Enumeration of Leukocytes. I. J. Yetwin.—p. 286.

New York State Journal of Medicine, New York

49:689-848 (April 1) 1949

Cor Pulmonale in Chronic Pulmonary Diseases of Industry. E. Mayer and I. Rappaport.—p. 825.
Some Clinical Features of Pneumoconiosis. J. B. Amberson.—p. 830.
Compensation Aspects of Pneumoconioses. Mary Donlon.—p. 833.
Aids in Diagnosis of Glaucoma. J. A. Inciardi.—p. 836.

49:849-976 (April 15) 1949

SYMPOSIUM ON PRIMARY CARCINOMA OF THE LUNG

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Pathology of Carcinoma of Bronchus. O. Auerbach.—p. 900.
Role of Bronchoscopy in Diagnosis and Treatment. L. H. Clerf and P. Herbut.—p. 907.
Cure Rate in Lung Cancer. R. H. Overholt and I. C. Schmidt.—p. 910.
Role of Physical Methods in Diagnosis. H. Kent.—p. 917.
Rehabilitation in Poliomyelitis. K. G. Hansson.—p. 923.
Present-Day Education in Physical Medicine. W. Bierman.—p. 927.
Five Years in Practice of Nineteenth Century New York Physician—Dr. William H. Van Buren. G. Rosen.—p. 932.
Elisha Bartlett, American Clinician. S. O. Sapin.—p. 935.
Interrelationship of Papilledema and Polycytemia. M. Axelrod and S. Epstein.—p. 939.
Leukemia, Lymphosarcoma and Hodgkin's Disease. M. M. Black, H. Bolker and W. E. Howes.—p. 943.

Southern Medical Journal, Birmingham, Ala.

42:263-358 (April) 1949

*Role of Massive Blood Transfusions in Management of Ruptured Uterus and Other Serious Obstetric Shock. C. J. Lund and F. O. Brumfield.—p. 263.
Silicosis. J. M. Frere.—p. 271.
Surgery of Upper Ureter for Obstruction. R. B. Henline.—p. 275.
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*Diagnosis of Chronic Recurrent Pancreatitis. W. G. Hersperger.—p. 289.
Current Status of Jet Injection. J. G. Hughes, R. G. Jordan and F. S. Hill.—p. 296.
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Head Injuries in Infancy and Childhood. B. Woodhall.—p. 310.
Repair of Painful Sacral Scars. M. M. Marks.—p. 319.
Aneurysm of Left Ventricle Secondary to Myocardial Infarction: Report of Case in Thirty-Five-Year-Old Man. H. L. Newbold, G. B. Wyatt and T. F. Frist.—p. 323.
Recent Advances in Understanding of Acute Episodes in Coronary Artery Disease. G. R. Meneely.—p. 325.
Changing Concept of Industrial Medicine. G. R. Rowntree.—p. 333.
Coordinating Lay Groups. F. J. Underwood.—p. 336.
Common Sources of Confusion in Psychiatric Matters. H. Cleckley.—p. 341.
Industrial Sporotrichosis. H. M. Robinson.—p. 343.
Further Observations on Suppository as Contraceptive. N. J. Eastman.—p. 346.

Blood Transfusion in Obstetrics.—Lund and Brumfield used massive transfusions of citrated whole blood in the treatment of 6 cases of serious obstetric shock and hemorrhage, 4 of which were due to spontaneous rupture of the uterus. Each patient received between 3,500 and 7,500 cc. of blood within a few hours, an amount which exceeded her normal calculated or estimated blood volume. Blood was given rapidly and efficiently without special apparatus by the technic of stripping the blood from the rubber tube of the transfusion set under positive pressure, starting the transfusion through a large gage needle. One hundred cubic centimeters can be given per minute through a single vein with this method, though usually two or more portals are required in severe shock. The immediate rapid restoration of circulating blood volume combined with prompt hemostasis prevented death in this group, which might well have had several fatalities. No untoward effects were noted from the transfusions. In 3 of the 4 patients the spontaneous rupture of the uterus was of the incomplete variety, and the rapid replacement of blood permitted the control of shock while preparations were being made for immediate surgical repair. The fourth patient presented an acute complete spontaneous uterine rupture during delivery. This patient was given successful immediate surgical treatment while moribund and while blood was being rapidly replaced under pressure by using both arms and one leg for the transfusions. Unless the loss of blood is completely replaced the puerperium may be further complicated by anemia, hypoproteinemia and not infrequently infection. The only stormy convalescence occurred in the patient who did not have her anemia corrected immediately after the hemorrhage. In all of the other patients the immediate postoperative blood count revealed hemoglobin levels equal to or higher than those before the operation.

Chronic Recurrent Pancreatitis.—Hersperger reports 33 cases of chronic recurrent pancreatitis in 23 men and 10 women between the ages of 18 and 67 years. Thirty-one of the patients had a history of severe pain. Of the 2 in whom pain was mild, 1 had evidence of calcification in the pancreas, the other had had diabetes for years and steatorrhea more recently. A vague, deep epigastric resistance is frequently reported, but only 5 of the 33 patients demonstrated an unquestionable mass. Serum amylase determinations were performed in 8 cases; in 7 the values were significantly elevated. The first requirement in the diagnosis of chronic recurrent pancreatitis is that the physician be familiar with the possible manifestations of the disease and consider it in the diagnosis along with other disorders which cause upper abdominal pain. It should especially be considered if appropriate studies have failed to reveal disease of adjacent organs when there is a long history of recurring attacks of severe, steady epigastric pain not relieved or only temporarily relieved by morphine sulfate. A history of alcoholism and the presence of disturbed carbohydrate metabolism is strong supportive evidence. Roentgen pictures taken to exclude

other diseases should be carefully scrutinized for evidence of calcification within the pancreas. Excess fat and meat fibers in the stools and definite evidence of reduced acinar function by duodenal drainage are not to be expected early but may become manifest as the disease progresses. It may be impossible to make a diagnosis between attacks unless some of the sequelae have developed. Chronic recurrent pancreatitis can be accurately demonstrated by the observation of elevated serum amylase or lipase values in the midst of an exacerbation.

Surgery, Gynecology and Obstetrics, Chicago

88:417-544 (April) 1949

Posttraumatic Vasomotor Disorders with Particular Reference to Late Manifestation and Treatment. H. B. Shumacker Jr. and D. I. Abramson.—p. 417.
Carcinoma of Vulva: Report of 313 Cases. J. P. Palmer, M. G. Sadugor and M. C. Reinhard.—p. 435.
Ureterosigmoid Anastomosis. J. J. Cordonnier.—p. 441.
Partial Gastrectomy in the War Years. C. A. Schoemaker.—p. 447.
Double Jejunal Lumen Gastrojejunal Anastomosis: Pantaloons Anastomosis. M. E. Steinberg.—p. 453.
Cervical Stump: Analysis of 123 Cases. J. B. Crawford, C. G. Collins and J. C. Weed.—p. 465.
Inguinal and Femoral Hernioplasty. C. B. McVay and B. J. Anson.—p. 473.
*Effectiveness of Dicumarol Prophylaxis Against Thromboembolic Complications Following Major Surgery: Four Years Survey: 3,304 Cases. W. D. Wise, F. F. Loker and C. E. Brambel.—p. 486.
Sliding Inguinal Hernia of Colon: Abnormal Peritoneal Folds and Simple Safe Method of Restoration. R. K. Brown.—p. 495.
Resection of Great Veins on Lateral Pelvic Wall. A. Brunschwig and T. S. Walsh.—p. 498.
Carcinoma of Cecum Complicated by Appendicitis or Para-Cecal Abscess. C. A. V. Burt.—p. 501.
Correction of Stress Incontinence by Simple Vesicourethral Suspension. V. F. Marshall, A. A. Marchetti and K. E. Krantz.—p. 509.
Intramedullary Bone Fixation in Pathologic Fractures. J. L. Ehrenhaft and R. T. Tidrick.—p. 519.
Prolonged Spinal Anesthesia, Use of Intrathecal Vasoconstrictor Substances. M. L. Brockmyer and T. S. McGowan.—p. 528.

Dicumarol® to Prevent Thromboembolic Complications.—Dicumarol® has been administered by Wise and co-workers to 3,304 patients in a prophylactic program. The initial dosage of the drug was 200 mg. administered on the second postoperative day. Subsequent doses were given on alternate days to maintain relative prothrombin activity of not under 40 per cent of normal. Dicumarolization was continued throughout the hospitalization period and discontinued when the patient was discharged. The average total consumption was 600 to 800 mg. The authors observed a significant reduction in the incidence of venous thrombosis following major abdominopelvic operation when oral administration of the anticoagulant, dicumarol,® was used prophylactically. Reduction in the mortality rate due to fatal embolism is statistically probable. Conservative depression of the prothrombin activity to 40 to 50 per cent of normal resulted in satisfactory prophylaxis and negligible hemorrhagic complications. No evidence of hepatic toxicity due to dicumarol® was noted as revealed by fibrinogen determinations. Rigid standardization of laboratory procedures for gaging the dicumarol® effect is essential for the success of a prophylactic program.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

57:143-180 (April) 1949

*Surgical Treatment of Decompensating Heart Disease and Angina Pectoris. P. G. Flothow.—p. 143.
*Comparative Study of Acute and Chronic Appendicitis in Pregnancy. E. S. Hoffman and M. Suzuki.—p. 150.
Water Balance. E. B. Speir and C. L. Wagner.—p. 158.
Criminal Abortion and Intestinal Destruction. W. E. Branch and C. L. Cooper.—p. 163.
Opisthotonus Fetalis. S. F. Nagyfy.—p. 165.
Hemangioma of Cervix: Case Report. J. F. McNabb and L. F. Bushnell.—p. 167.
Obstetrical Anesthesia at the Cedars of Lebanon Hospital: Ten-Year Survey. G. S. Harris.—p. 169.
Antihormone Formation in Man Following Chorionic Gonadotropin. J. H. Leathem and J. T. Bradbury.—p. 173.

Angina Pectoris.—Flothow treated 23 patients with angina pectoris by paravertebral alcohol injection of the dorsal sympathetic ganglions from the first to the fifth either on the left side or on both sides. Seventeen patients were decidedly improved, obtaining from 75 to 100 per cent relief of their pain. Other types of surgical procedures on the sympathetic nerves in the treatment of angina pectoris are cervical sympathectomy, cervicodorsal sympathectomy, dorsal ganglionectomy and ramisectomy, and intraspinal dorsal root section. The type used by the author consists of removal of the stellate ganglion and the first three or four dorsal ganglions, but it would seem that the type of operation preserving the inferior cervical and first dorsal ganglions, thus avoiding a Horner's syndrome, would appear to be the operation of choice. Sympathectomy has been ultimately satisfactory in at least 75 per cent of the patients. Unsatisfactory results were observed to occur in women generally, in those men in whom the diagnosis perhaps was not correct, and in patients with addiction to morphine and its derivatives. Three cases of angina pectoris with concomitant decompensating cardiac disease in men aged 63, 69 and 46 are reported by the authors. Two of them were treated with paravertebral alcohol injections and the third one with sympathectomy. The treatment succeeded not only in relieving the anginal pain but also in clearing up the decompensation without further medication. Patients without irreversible changes, and in whom the decompensation can still be relieved by bed rest and medication, can be enabled to carry on normal lives, without recurring decompensation, by operation on the sympathetic ganglionated chain carrying the sympathetic innervation to the heart and its blood vessels.

Appendicitis in Pregnancy.—Hoffman and Suzuki operated on 54 pregnant women with a preoperative diagnosis of appendicitis. Twenty-three were cases of acute appendicitis and 31 were cases of chronic appendicitis. In the latter group elective appendectomy was performed on 18 patients and emergency appendectomy on 13. The history and symptomatology in the acute series and in the emergency chronic group were similar. In the emergency chronic group, 8 patients were followed and none had any recurrence of symptoms after the operation; 11 patients in the elective group were followed, and 8 remained symptom free. The right rectus incision was most frequently employed in both series of cases. The McBurney or the Davis incision is probably the incision of choice during the last six months of pregnancy. In the acute appendicitis series, the appendix was observed to be retrocecal in 11 and fixed by adhesions in 3 as compared to 3 retrocecal and 4 fixed by adhesions in the chronic group. The seriousness of the "fixed" appendix is apparent from the fact that three of four abortions which occurred within the first three postoperative days were in this group. In 4 patients in the acute group fetal loss occurred before the patients left the hospital as compared to 2 patients in the chronic group. Symptoms of threatened abortion occurred in 3 of the 18 patients in the acute series and in 4 of the 28 patients of the chronic series who were discharged from the hospital undelivered. These symptoms were controlled by the free use of sedatives and small doses of progesterone, the latter of questionable value. Follow-up studies on 18 patients in the acute series and on 24 patients in the chronic series showed that 5 of the undelivered patients in the acute series terminated their pregnancies before full term, while in the chronic series all 24 patients went to full term. The high incidence of fetal loss in the acute series is due to the high incidence of spontaneous abortion and premature labor. In acute appendicitis in pregnancy appendectomy is the procedure of choice, regardless of the period of gestation. The authors do not believe that cesarean section should precede the appendectomy in the presence of acute appendicitis with perforation and generalized peritonitis.

Yale Journal of Biology and Medicine, New Haven

21:263-364 (March) 1949

New Theory of Mutation and Origin of Cancer. L. C. Strong.—p. 292.
Unusual Case of Hypersensitiveness to Mercurial Diuretic. J. K. Meneely Jr.—p. 301.
Instrumentation for Laboratory Exercises in Basic Electrophysiology. A. Mauro and D. H. Barron.—p. 305.
Relationship Between pH Tolerance, Virulence and Proteolytic Enzymes in Bacteria: II. Shigella. J. M. Leise.—p. 313.
Studies in Experimental Frostbite: III. Evaluation of Several Methods for Early Treatment. R. E. Lempke and H. B. Shumacker Jr.—p. 321.
Review of Animal Experimentation in Infectious Hepatitis and in Serum Hepatitis. J. W. Colbert Jr.—p. 335.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Journal of Industrial Medicine, London

6:65-124 (April) 1949

*Vesical Tumors Induced by Chemical Compounds. M. W. Goldblatt. —p. 65.
Manganese Pneumonitis: Further Clinical and Experimental Observations. T. A. L. Davies and H. E. Harding.—p. 82.
Changes in Lungs Produced by Natural Graphite. H. E. Harding and G. B. Oliver.—p. 91.
Sickness Absence Due to Peptic Ulcers. R. Doll and M. M. Buckatszch. —p. 100.

Vesical Tumors Induced by Chemical Compounds.—Goldblatt analyzes cases of vesical tumors detected among workers in two factories in Britain which were engaged in the manufacture of a wide variety of organic intermediates and dyestuffs, rubber chemicals, textile finishing agents, organic primaries and many other compounds. In the years 1934-1947, inclusive, a total of 99 cases of vesical tumor were detected, of which 59 resulted in death during the fourteen years of observation. The total number of workers in these factories increased from 2,025 in 1934 to 4,163 in 1947. The mean period from first entry into the industry until discovery of the tumor was approximately nineteen years. Although of the primary aromatic amines only beta-naphthylamine has been shown experimentally to produce bladder tumors in dogs, evidence is presented that cases arise not only among workers who have been working exclusively with beta-naphthylamine but also among those working exclusively with aniline, benzidine and alpha-naphthylamine (containing small percentage of the beta-isomer). Tumors arising in workers who have been working with beta-naphthylamine or more than one of the amines are more likely to be malignant from the start than those arising in workers working with only one of these amines. Recurrences are characteristic of the disease and many appear from as little as a month or two after operation to as long as seven years after. Metastases were found in only 5 cases coming to necropsy, which indicates that they are relatively uncommon. The author mentions possible improvements in processing which could contribute to elimination of the disease. It is held that the so-called amino carcinogens are only indirectly responsible for the tumor formation in that they sensitize or potentiate the tissue to the true carcinogen. The amino potentiator (carcinogen as it is now called) is believed to be carried in the urine.

British Journal of Ophthalmology, London

33:197-260 (April) 1949

Experimental Studies on Pathogenesis and Treatment of Ocular Tuberculosis. A. C. Woods.—p. 197.
Vascular Action of Pilocarpine, Eserine, Adrenaline and Atropine, and Their Influence in Primary Chronic Glaucoma. G. Cristini.—p. 228.
Slit-Lamp Examination of Vitreous and Fundus. H. Goldmann. —p. 242.
Blood-Vessel Formation in Cornea. F. W. Campbell and I. C. Michaelson.—p. 248.

British Journal of Tuberculosis, London

44:1-22 (Jan.) 1949

Pulsus Paradoxus and Pleurisy. W. E. Gibb.—p. 1.
Tuberculoma of Lung Masquerading as Encysted Pleural Effusion. N. Wynn-Williams.—p. 6.
Key to Classification of Pulmonary Tuberculosis. M. Sekulich.—p. 12.
Pneumomediastinum Complicating Artificial Pneumoperitoneum. J. B. Morrison.—p. 18.

British Medical Journal, London

1:645-690 (April 16) 1949

In Praise of Idleness. S. Ogilvie.—p. 645.
Discomforts of Childbirth. G. D. Read.—p. 651.
Non-Specific Effects of Impure Penicillin. J. Ungar.—p. 654.
Needle Biopsy of Liver, with Special Reference to Modified Gillman Technic. R. Terry.—p. 657.
Severe Renal Failure After Administration of Apparently Compatible Blood. A. C. Buchan and J. Wallace.—p. 660.
Dysentery in South Persia. I. S. Stewart.—p. 662.
Further Experiences with Ethinyl Estradiol in Suppression of Lactation. T. N. A. Jeffcoate and Betty Hargreaves.—p. 664.
Metatarsus Quintus Valgus. H. Davies.—p. 664.

Journal of Hygiene, London

46:351-470 (Dec.) 1948. **Partial Index**

*Smallpox in Tripolitania, 1946: Epidemiologic and Clinical Study of 500 Cases, Including Trials of Penicillin Treatment. C. W. Dixon. —p. 351.
Epizootic Behavior of Mousepox (Infectious Ectromelia of Mice): Course of Events in Long-Continued Epidemics. F. Fenner.—p. 383.
*Survival of Foot-and-Mouth Disease Virus in Meat and Offal. W. M. Henderson and J. B. Brooksby.—p. 394.
Hemolytic Disease of Newborn Foals Due to Iso-Immunization of Pregnancy. R. R. A. Coombs, R. C. Crowhurst, F. T. Day and others. —p. 403.
Retention of Methallyl Chloride and Methyl Bromide by Fumigated Grain. N. van Tiel.—p. 431.

Smallpox in Tripolitania—Dixon describes methods used in two epidemics of smallpox which occurred in Tripolitania during 1946. Control was effected by the "expanding ring" method instead of mass vaccination of the population. The "expanding ring" vaccination was organized on the supposition that smallpox behaves like other droplet infections and that the maximum incidence would be expected in the family, the chance of infection decreasing as distance from the family center increased. In each case the family was vaccinated first, then the inhabitants of the surrounding tents together with close contacts such as relatives, next the village or group of tents and so on, the area covered increasing for five days, after which revaccination started again at the center concurrently with a search for cases. A clinical study was made of 500 patients who were admitted to hospital. Controlled experiments were made on the use of penicillin in treatment. Although it is without effect on the viremia and in general does not significantly affect mortality, it has the power of suppressing suppuration and reducing the effect of secondary sepsis. It also minimizes the amount of permanent scarring of the skin. Evidence is presented to show that the period of maximum infectivity is the stage of the preeruptive fever. The mildest conditions are infectious, but only for a short time. The virus contained in dried scabs is not considered to be an important source of infection; it may be modified in some way by passage through the skin. Although not protected by successful vaccination many contacts showed a considerable resistance to infection. Among the older persons this may have been due to previous clinical or subclinical attacks. Evidence is produced to show that among younger persons many were relatively refractory to vaccination and experienced the disease in a different way, suggesting that there is natural partial immunity to smallpox in this population.

Survival of Virus of Foot and Mouth Disease in Meat.—According to Henderson and Brooksby it has long been known that the virus of foot and mouth disease can survive in certain animal tissues at temperatures used for chilling and freezing of meat. During the war of 1939-1945 some changes took place in the methods of handling meat for importation into Great Britain from South America. One change from previous practice adopted with a small percentage of the meat was the "quick freezing" of boned quarters in special molds before the development of rigor mortis. As this might produce conditions favorable for the survival of foot and mouth disease virus, further research was necessary. It was found that the survival of virus is closely associated with the hydrogen-ion concentration of the tissue; thus the acidity of rigor mortis of muscular tissue rapidly causes inactivation. Quick freezing of beef suspends acid formation and active virus was demonstrated for as long as the meat was kept frozen. Thawing of quick-frozen meat initiates the suspended acid formation at an accelerated rate and rapidly produces a medium unsuitable for virus survival. Liver, kidney, rumen, lymph node and blood from diseased cattle have all been shown to be highly infective and to remain so if stored frozen. Acid formation in these tissues and in blood is not on the same scale as in muscle, and prolonged survival of virus is more likely even with delay in freezing and after thawing. This remains true of lymph node and of residual blood in vessels of a carcass in which the development of rigor mortis is complete. Feeding of infective offal to swine under experimental conditions resulted in the appearance of the disease.

Journal of Physiology, Cambridge

108:1-116 (March) 1949. **Partial Index**

New Method for Measuring Arterio-Venous Oxygen Difference by Means of Photoelectric Colorimeter. B. Issekutz Jr., G. Heténvi Jr. and I. Feuer.—p. 9.
*Simplified Method for Determination of Circulating Red-Cell Volume with Radioactive Phosphorus. E. B. Reeve and N. Veall.—p. 12.
Measurement of Temperature at Eardrum During Caloric Test of Labyrinth. J. J. Groen and L. B. Jongkees.—p. 33.
Intensity Discrimination of Central Fovea Measured with Small Fields. L. C. Thomson.—p. 78.
Relation Between Motor and Inhibitor Actions of Acetylcholine. J. H. Burn and J. R. Vane.—p. 104.

Radioactive Phosphorus in Estimation of Red Cell Volume.—Reeve and Veall describe experiments which were carried out to establish and to test a method in which the radioactive red cells were washed free from radioactive plasma before they were injected and in which the radioactive measurements were carried out on liquid blood samples by means of a specially designed counter. The total red cell volume in man is measured from the dilution of injected washed red cells, labeled in vitro with P_{32}. The red cells are prepared by incubating whole blood with P_{32} and afterwards washed almost free of their radioactive plasma. After injections of suspensions of such washed red cells, P_{32} is lost slowly from the circulation. The results from the method agree with results of other reliable methods. The method has also been checked in vitro. A specially designed Geiger-Müller counter taking liquid samples simplifies the necessary manipulations of standards and samples. Apart from knowledge of radioactive technic, the method requires no great technical skill.

Lancet, London

1:637-676 (April 16) 1949

Wertheim's Operation in Retrospect. V. Bonney.—p. 637.
Excretion of Chloride and Sodium After Surgical Operations. A. W. Wilkinson, B. H. Billing, G. Nagy and C. P. Stewart.—p. 640.
Treatment of Stammerer in Secondary Stage of Stammering. M. C. Crickmay.—p. 644.
Factors Influencing Maintenance of Antitoxic Immunity. M. Barr and A. T. Glenny.—p. 646.
Intestinal Rupture Following Non-Penetrating Injury. G. Flavell. —p. 649.
*Gynecomastia During Treatment with Amphetamine. P. H. Tooley and C. Lack.—p. 650.
Fibrocystic Disease of Pancreas in Infant. G. G. Jones.—p. 651.
Estimation of Ergothioneine in Urine by Paper Partition Chromatography. E. Work.—p. 652.

Gynecomastia During Treatment with Amphetamine. According to Tooley and Lack amphetamine sulfate has been recommended for a wide diversity of conditions, including depressive states, fatigue, epilepsy, narcolepsy, certain behavior disorders of children, dysmenorrhea, enuresis, migraine and obesity. Some male patients complained of bilateral, slightly tender, swelling of their breasts while they were taking amphetamine sulfate. The authors asked all male patients receiving this drug whether they had noted enlargement of their breasts. A surprising number admitted that they had noticed it. The authors regard it as unlikely that amphetamine sulfate has a direct effect, since it bears no chemical similarity to the sex hormones. It appears to them most probable that it acts at a pituitary hypothalamic level, leading to the increased production of estrin, probably by the adrenals, and/or a reduction in testosterone, with the result that the estrin-testosterone ratio is altered. This is purely speculative. The inference is that the effects described were due to an impurity in the amphetamine sulfate, which had considerable estrogenic potency. In the course of its preparation amphetamine sulfate passes through a chemical process in which substances closely related to the estrogens are formed.

Medical Journal of Australia, Sydney

1:333-368 (March 12) 1949. **Partial Index**

Pulmonary Infarction and Anticoagulant Therapy. A. W. Morrow. —p. 341.
Psychosomatic Aspects of General Medicine. H. R. Love.—p. 347.
Diagnosis of Eighth Nerve Tumor. G. Phillips.—p. 351.
Some Aspects of Subacute Bacterial Endocarditis. E. F. Gartrell. —p. 353.

Deutsche medizinische Wochenschrift, Stuttgart

74:417-448 (April 8) 1949. **Partial Index**

*Superfecundation in Human Beings. H. Heberer.—p. 417.
*Preliminary Examinations and First Results in Connection with BCG Vaccination of Children 6 to 14 Years of Age in a Rural District. F. Lütgerath, B. Bergmann and H. Stöppler.—p. 419.
Results of Treatment of Acute Pneumonias: Report on 1,431 Cases from 1936 to 1946. H. Hackerott.—p. 422.
Roentgenogram of Dental Focus of Infection. E. Fröhlich.—p. 426.
Advisability of Operation for Hallux Valgus. H. Richter.—p. 430.
Bacterial Flora in Gynecologic Operations. P. Bernhard.—p. 431.

Superfecundation in Human Beings.—Heberer differentiates between superfecundation and superfetation. Superfecundation results when as the result of different acts of copulation several ova maturing during the same period of ovulation become fertilized. Superfetation would result if an ovum from a later period of ovulation would be fertilized. The possibility of superfetation has been denied, even in the presence of a double uterus, since ovulation ceases during pregnancy. Superfecundation, however, is regarded as possible in human beings. The author reviews a lawsuit about the paternity of twins, in which it was contended, on the basis of blood group tests, that the defendant could not have been father of one of the twins, that is, that the twins must have had two fathers; and this in turn would prove the possibility of superfecundation in human subjects.

BCG for Protection Against Tuberculosis.—According to Lütgerath and associates vaccination against tuberculosis is becoming more urgent in Germany because of the increase in the tuberculosis morbidity in adults and children. The offer of the Red Cross of Denmark to perform vaccinations with BCG was therefore gratefully accepted. The authors report on the examinations made preparatory to such vaccinations and on the first results of the after-examinations in children 6 to 14 years of age. The percentage of natural infection is listed for the different age groups. It has reached 47 per cent in those 14 years of age. The authors stress the advisability of roentgenologic controls for children with positive reactions and believe that all inhabitants of the district should be subjected to examination before the roentgen screen, because in this way possible sources of infection would be detected. Particular attention should be given to bovine sources of infections, since the search for human sources frequently remains fruitless. There were practically no undesirable reactions from the vaccination. The vaccination pustules were of normal size. The reactions to patch tests following the vaccination were usually strong and must be regarded as the expression of a favorable allergic condition. Patch test controls should be made annually in order to obtain information about the duration of positive reactions and the duration of protection conferred by the BCG vaccination. In view of the excellent tolerance for BCG, the authors consider it advisable to extend this vaccination to other age groups.

Encéphale, Paris

38:97-144 (No. 3) 1949

*Electro-Encephalographic Study of Epileptic Cortical Foci. H. Gastaut and M. B. Dell.—p. 97.
*Treatment of Schizophrenia by Massive Withdrawal of Cerebrospinal Fluid Followed by Injection of Air. J. Borel and P. Poujol.—p. 108.
Postemotional Acute Porphyria; Exophthalmos; Extensive Paretic Syndrome with Psychic Disturbances. L. Marchand and J. de Ajuriaguerra.—p. 113.

Epileptic Cortical Foci.—Gastaut and Dell performed encephalographic studies on 700 patients with epilepsy. Records were made with bipolar leads. In 119 patients, 17 per cent, localized unilateral abnormality was observed. Thirty-one of them presented the symptomatic type of epilepsy, i. e., tumor or cranial traumatism, and were not included in the report. The remaining 88 patients with unilateral abnormality apparently were the "cryptogenic" epileptic type. In 62 of these the abnormality focalized in the narrow sense of the word, and in 26 it was localized in a limited region of one hemisphere. Spikes, complex spikes and sharp waves are the types of unilateral abnormality which may be observed in patients with focalized epilepsy. Delta waves and 2 per second alternating waves and spikes were observed also, but in patients with the "localized" type of epilepsy. The spikes and sharp waves

practically always are produced by cortical or immediately subcortical lesions, such as corticomeningeal scars resulting most frequently from old truma, localized atrophic lesions and inflammatory, vascular or neoplastic lesions causing a highly localized cortical destruction. Among the focalized anomalies a focus with spikes or sharp waves constitutes the best indication for surgical intervention. The 2 per second alternating waves and spikes or degenerated waves were observed frequently with regional cortical atrophy or with porencephalic foci accompanied by evident clinical signs. Delta waves, when accompanied by spikes or sharp waves, indicate a localized cortical disturbance, degenerative or edematous, and the sharp waves indicate an adjacent or superimposed irritative focus. Two eventualities may be envisaged concerning the localized paroxysmal categories with harmonious monorhythmic or polyrhythmic waves: (1) Transitory paroxysms with fairly rapid waves often associated with a localized clinical attack. They constitute an electrical expression of this attack, thus assuming a great value for localization. (2) Repeated paroxysms with slow waves or alternating waves and spikes in the absence of any clinical manifestation, which are less valuable for localization.

Treatment of Schizophrenia.—Borel and Poujol treated 17 patients with schizophrenia by repeated withdrawal of 10 cc. of cerebrospinal fluid followed by injection of 10 cc. of air, with thiopental sodium anesthesia. The total amount of withdrawn cerebrospinal fluid and of injected air, respectively, varied from 60 to 100 cc. There were no untoward reactions. The duration of the disease in 9 patients was not more than thirteen months. There were 4 complete recoveries followed up for more than one year. There was persistent but only partial improvement in 1 patient, 1 recurrence after several months in another patient and 3 failures. The duration of the disease in 8 patients was two to seventeen years. There were 6 failures, and 2 patients had temporary recurrences, 1 after two years and the other after four years. The sudden disturbance of the dynamics of the cerebrospinal fluid may have its repercussions on the cerebral vascular system; the injected air may exert mechanical excitation of the walls of the third ventricle and thus may stimulate an inhibited function. The massive withdrawal of cerebrospinal fluid combined with electroshock and insulin treatment should be given a trial in cases of schizophrenia of less than two years' duration before the patient is considered incurable.

Nordisk Medicine, Stockholm

41:531-574 (March 25) 1949. **Partial Index**

*Tubular Nephritis. H. Bergstrand.—p. 531.
Small Heart. P. Dundas.—p. 536.
Combination of Psychotechnical Method and Electroencephalography. B. Bjerner and O. Steinwall.—p. 545.
Automatic "Respiration Exposer" in Roentgenography of Thorax in Infants. P. E. Heikel.—p. 546.
Status Asthmaticus in Adults Treated with Manual Compression of Thorax. L. Epstein.—p. 549.

Tubular Nephritis.—Bergstrand discusses proximal and distal tubular nephritis. He designates the renal changes characterized by degeneration of the tubular epithelium without notable involvement of the glomeruli as tubular nephritis rather than nephrosis, as the degenerative or necrotic changes may be followed by pronounced inflammatory reactions in the interstitial tissues. The clinical symptoms are oliguria or anuria with azotemia and sometimes increased blood pressure. The picture appears in many disorders which are followed by muscle or blood degeneration: after incompatible blood transfusion, in acute malaria due to Plasmodium falcifarum, grave burns with destruction of red blood corpuscles, heat stroke with excessive hemorrhage, traumatic and atraumatic ischemic muscle necrosis and intoxications which cause hemolysis or bleeding, and intoxications with certain substances known to cause blood or tissue necrosis, as sulfonamide drugs. There are generally more or less pronounced signs of shock. Pathologically the organs show capillary distention, frequent centrilobular liver necrosis, necrosis in other organs and hemorrhages in different organs. The renal cortex is usually pale and anemic and the parenchyma dark red and hemorrhagic. The changes are focal. Tubular nephritis is ascribed to toxic influences, acid urine and insufficient blood supply to the kidneys. All three factors may play a part. The most characteristic form of proximal tubular nephritis may be that caused by mercuric chloride intoxication. Intoxication with oxalic acid may cause this form of tubular nephritis. Administration of certain amino acids may produce similar changes.

Revista de la Asociación Méd. Argentina, Buenos Aires

63:53-90 (Feb. 15-28) 1949. **Partial Index**

*Experiments on Streptomycin. Resistance of Tubercle Bacilli. R. F. Vaccarezza, A. Centrángolo and R. Cucchiani Acevedo.—p. 53.

Tubercle Bacilli Resistance to Streptomycin.—Vaccarezza and collaborators carried on in vitro determinations of the sensitivity of tubercle bacilli to streptomycin in two series of 30 and 60 strains. Twenty-nine of the 30 strains of tubercle bacilli from patients who had not previously received streptomycin were sensitive to the drug in a concentration of 0.1 to 1 mg. per cubic centimeter of the culture medium, and 41 out of 60 strains of tubercle bacilli from patients in the course of streptomycin therapy were resistant to the drug in a dose of 10 mg. or more per cubic centimeter of the culture medium. Resistance to streptomycin occurred before 50 Gm. had been administered in 4 cases, before receipt of a total dose which varied between 50 and 100 Gm. in 16 cases and after administration of more than 100 Gm. in 21 cases. Late resistance appeared in 2 cases twenty-two days and four months after discontinuation of a total dose of 20 and 13 Gm., respectively. Determinations of the sensitivity of tubercle bacilli were repeated in 10 patients with resistant strains for a period of one to five months. Resistance to the drug persisted in all strains. In the group of patients with sensitive strains of tubercle bacilli who were receiving streptomycin, 1 patient had had a total dose of 200 Gm., 5 patients had had a total dose which varied between 150 and 200 Gm. and 7 patients had had a total dose which varied between 100 and 150 Gm. There was a correlation between the results of the bacteriologic research and of the therapeutic effect, namely, cure of 12 patients with sensitive strains and failure of the treatment of 40 patients with resistant strains. The treatment failed in 7 patients with sensitive strains. Improvement of a patient with a sensitive strain of tubercle bacilli progressed without interruption after the occurrence of resistance.

Revue d'Hématologie, Paris

4:1-174 (No. 1) 1949. **Partial Index**

Leukemia Associated with the Presence of Eosinophils? A. Piney.—p. 3.
Application of Examination of Blood Groups to Paternity Search. L. Hirszfeld and F. Milgrom.—p. 6.
Heredity of Blood Groups P in 85 English Families. Ruth Sanger, Sylvia D. Lawler and R. R. Race.
Human Blood Groups "Kell"; Gene Frequencies and Genetic Research. Ruth Sanger, Doreen Bertinshaw, Sylvia D. Lawler and R. R. Race. —p. 32.
*Results of Treatment of 160 Newborn Babies with Hemolytic Anemia by Exchange Transfusions. J. J. van Loghem and H. L. J. M. Bartels. —p. 36.

Exchange Tranfusions in Newborn Babies.—Van Loghem and Bartels treated 160 newborn babies with hemolytic anemia with repeated and massive replacement transfusions, using Diamond's technic but employing a rubber catheter instead of the plastic catheter. Heparinized blood was used in the majority of the cases. The catheter and the syringes must be washed regularly during treatment with a weak heparin solution to prevent the formation of clots. Thirty-six of the infants died, a mortality rate of 22.5 per cent. Seven of the deaths were not related directly to the hemolytic anemia. When these latter cases are eliminated, the mortality rate is 18.1 per cent. In the remaining 29 instances death resulted from kernicterus in 9, fetal dropsy in 3, incompatible blood in 3, hemorrhages in the visceral organs in 5, premature birth in 1 and belated treatment in 1; in 7 cases the cause of death was unknown. The mortality rate in the group of treated infants was compared with that of a group of infants with erythroblastosis fetalis in the same families who were not treated by exchange transfusions. The

mortality rate in the latter group was 73.3 per cent for the infants with severe icterus and 63.5 per cent if those with mild icterus were included. The mortality rate was reduced from 63.5 per cent to 18.1 per cent by the application of exchange transfusions. It is the only treatment which has thus far proved effective.

Schweizerische medizinische Wochenschrift, Basel

79:237-260 (March 19) 1949

Instruction in Surgery. O. Schürch.—p. 237.
*Meningitis Myalgica; Serous Meningitis in Epidemic Myalgia. O. Gsell.—p. 241.
Experimental Studies Concerning the Nature and Pathogenesis of Angina Pectoris and Myocardial Infarction. S. Hirsch.—p. 245.
Progressive Defense Against Venereal Diseases. H. Rotter.—p. 249.
Arterenol, Hormone of Adrenal Marrow and Chemical Transmission Substance of Sympathetic Nerve Stimuli. P. Holtz and H. J. Schümann.—p. 252.

Serous Meningitis in Epidemic Pleurodynia.—Gsell reports 7 cases of serous meningitis complicating epidemic pleurodynia in 5 patients between the ages of 16 and 40 and in 2 children aged 5 and 7. These cases occurred in the Swiss canton of Saint Gallen during the summer and autumn of 1948. The term myalgic meningitis has been suggested for this type of virus meningitis. Serous meningitis may occur in single cases of familial epidemic pleurodynia as in 1 of the author's cases in a family of 10 with pleurodynia, or it may occur sporadically without additional incidence in the same household as in 4 of the author's cases. In all 7 patients the meningitis occurred during the second bout of the disease between the third and sixth day. The clinical picture corresponded with that of a more or less intensive meningitis without pronounced psychic changes. There were no encephalitic complications; the maximum cerebrospinal fluid cell count varied from 17 to 408. Neutrophils were predominant in the cerebrospinal fluid in the early stage and lymphocytes in a later stage. There was a slight increase in albumin content; the sugar content was normal. The blood picture showed a tendency to leukopenia. The blood sedimentation rate was only slightly increased. The duration of the meningitis varied from one to three weeks. All patients recovered without any sequelae. Treatment consisted of rest in bed, lumbar puncture and administration of analgesics. Chemotherapy and antibiotics are of no value. The increased incidence of epidemic pleurodynia in Central Europe during the last year is emphasized.

Strasbourg Médical

109:55-64 (Feb. 15) 1949

*Analytic Study of Problem of Hemogenia. R. Voegtlin and J. Cherrier.—p. 55.
Inflammation of Middle Ear and Digestive Disturbances of Suckling Babies; Therapeutic Indications. P. Rohmer, E. Schneegans and C. Wild.—p. 61.

Hemogenia.—Voegtlin and Cherrier report 2 cases of hemogenia, 1 in a man aged 34 with intestinal hemorrhages, secondary anemia and ecchymoses from the slightest contusion and a second in a woman aged 26 with menorrhagia, profuse hemorrhages after extraction of teeth, epistaxis, ecchymoses on the lower extremities and purpura on the upper part of the breast. Splenectomy was performed in both cases, resulting in disappearance of hemogenia. Eleven to twenty months after the intervention the number of thrombocytes was about the same as that before intervention. The results were identical in both patients, although they differed with regard to the clinical picture, the hematologic reaction immediately following the intervention, the lesions of the spleen and the bone marrow pattern. Thrombopenia is an epiphenomenon in the pathologic changes of chronic idiopathic thrombopenic purpura, which is essentially a vascular disease. In the majority of the cases the thrombopenia depends on changes in multiplication and maturation of the megakaryocytes, but there does not exist a specific pathognomonic type of cytologic change in the bone marrow and a single morphologic type of hemorrhagic spleen. Although splenectomy induces clinical improvement in hemogenia by restoring hemostasis and capillary resistance, it does not necessarily cause the return of the number of thrombocytes and the condition of the megakaryocytes to normal. The reticuloendothelial system after splenectomy exerts a vicarious action on the morphologic aspects of the blood and the blood-forming tissues which may make up partly or entirely for the absent spleen. The increase in the number of megakaryocytes in the bone marrow and the presence of forms with abnormal maturation are of definite aid in the diagnosis of Werlhof's disease and warrant a favorable prognosis for splenectomy.

Ugeskrift for Laeger, Copenhagen

111:139-164 (Feb. 10) 1949. **Partial Index**

*Sulfonamide Nephritis. R. Christensen.—p. 139.
Popper's Operation for Otosclerosis. Results. I. P. Vald.—p. 145.
Use of Nitrogen Mustard. A. Videbaek.—p. 147.

Nephritis Due to Sulfonamide Drugs.—Christensen states that in the grave renal complications which may occur with sulfonamide drug therapy the clinical picture is characterized by shock, vomiting and renal symptoms in the form of oliguria, hyperazotemia, changes in the chemical content of the blood and albuminuria. There are torpidity and dulness with a rise in temperature and often conjunctival and cutaneous signs of hypersensitivity. Four cases of nephritis due to sulfonamide drugs are described. In 2 cases death occurred from uremia; 2 patients were discharged as subjectively well, but impairment of the renal function still persisting on control after four months show the grave damage that the kidneys are exposed to in intoxication due to sulfonamide drugs. The small dose of sulfonamide drugs which can cause the disorder suggest an allergic rather than a toxic pathogenesis. In the fifth case there were also torpidity and dulness together with decided edema; death was due to uremia. Microscopic examination did not show definite allergic changes such as were seen in the first 2 cases. The patient had received sulfonamide drugs for some time. The blood transfusion given immediately before the onset of the symptoms was accompanied by signs of incomplete compatibility. If the allergic inflammatory changes in the kidneys in the first cases are to be taken as a sign that the nephritis due to sulfonamide drugs is the result of hypersensitivity, the absence of these phenomena in the last case must point to lower nephron nephrosis resulting from the blood transfusion.

Wiener klinische Wochenschrift, Vienna

61:209-224 (April 8) 1949. **Partial Index**

*Vagotomy as Intervention for Alleviation of Pain in Inoperable Carcinoma of the Stomach. F. Mandl.—p. 209.
Choice of Indifferent Electrode or Electrode Distal to Heart in Thoracic Wall-Electrocardiogram in Man. W. Breu.—p. 211.
New Mechanism of Regulation for Coordination of Respiration and Circulation. H. Schröcksnadel.—p. 214.
Psychic Changes After Prefrontal Leukotomy. E. F. Pakesch.—p. 215.

Vagotomy in Inoperable Cancer of the Stomach.—Mandl performed vagotomy in 4 patients, 3 men and 1 woman between the ages of 59 and 71, with inoperable carcinoma of the stomach. Gastrectomy was not feasible in any of the 4. There was no stenosis. Relief of pain resulted in all. Except for a temporary increase in weight of 4 to 5 Kg. the course of the disease was not changed. The temporary improvement was due to the pain-alleviating effect of the vagotomy and to the return of appetite. Postoperative disturbances, such as diarrhea, did not occur. In the absence of stenosis, vagotomy is to be preferred to any other palliative intervention on the stomach. In the presence of stenosis considerable improvement in inoperable carcinoma of the stomach may be expected from vagotomy combined with gastroenterostomy. In 1 patient the repugnance to meat disappeared after the vagotomy. The alleviation of pain resulting from vagotomy may be explained by the simultaneous interruption of the splanchnic nerve, for, in cutting the right vagus nerve, one may also sever sympathetic fibers leading to the semilunar ganglion. There is also the possibility that spasms of segments of the gastric wall may be responsible for the pain of carcinoma of the stomach. The occurrence of atony after vagotomy may explain the pain-alleviating effect of the operation in cases of carcinoma of the stomach and in cases of ulcer.

Book Notices

Current Therapy 1949: Latest Approved Methods of Treatment for the Practicing Physician. Howard F. Conn, M.D., editor. Consulting Editors: M. Edward Davis and others. Cloth. Price, $10. Pp. 672. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1949.

This book represents an attempt to provide for the practitioner the latest method of treatment for a variety of diseases. A board of twelve consulting editors and over two hundred physicians have contributed to the book. The contents are divided into fourteen sections: Infectious diseases, diseases of the digestive system, diseases of metabolism and nutrition, diseases of the endocrine system, diseases of the urogenital tract, venereal diseases, diseases of allergy, diseases of the skin, diseases of the respiratory system, diseases of the cardiovascular system, diseases of the blood and spleen, diseases of the nervous system, obstetric and gynecologic diseases and diseases due to physical and chemical agents. The discussions are brief, with a minimum of wasted words. However, the essentials of the method of treatment proposed by the contributors are sufficiently complete for the reader to obtain a clear understanding of the therapeutic problem. This book does not present a review of the literature; it presents "a method that has been endorsed and is currently used by a competent authority." In many instances the methods of two or more authorities for treating a single disease have been included.

Essentials of Gynecologic Endocrinology [with Sections on the Male]. By Gardner M. Riley, Ph.D., Assistant Professor of Obstetrics and Gynecology, University of Michigan Medical School, Ann Arbor, Mich. Paper. Price, $3. Pp. 205, with 35 illustrations. Caduceus Press, Box 17, Ann Arbor, Michigan, 1948.

This volume includes three sections: (1) Endocrine Physiology, (2) Clinical Aspects and (3) Diagnostic Procedures, Sex Hormone Chemistry and Endocrine Preparations, all pertaining to the function and dysfunction of the female reproductive system. There are included also chapters on the endocrine glands other than sex, such as the adrenals, thyroid and pancreas, and also chapters on the clinical aspects of other endocrine diseases, such as Symmond's disease, Cushing's syndrome and disorders of the testes. Certainly, knowledge of the male endocrine dysfunctions is necessary in the treatment of sterile couples, but the other discussions are obviously not essential in a book on gynecologic endocrinology. The material in this volume is concentrated and may be considered to be an excellent outline of our knowledge of gynecologic endocrinology. The descriptive material is too scant for beginners such as students but more appropriate for physicians who have some knowledge of the subject and who would appreciate a condensation for review purposes. It is especially suited for gynecologists who will find this a handy volume with which to refresh their knowledge of the sex hormones and functional gynecologic disorders. There is a bibliography at the end of each chapter for reference purposes.

On the Contributions of Hugh Owen Thomas of Liverpool, Sir Robert Jones of Liverpool and London, John Ridlon, M.D., of New York and Chicago to Modern Orthopedic Surgery. By H. Winnett Orr, M.D., Chief Surgeon, Nebraska Orthopedic Hospital, Lincoln, Nebraska. With a Supplement on Ridlon and His Share in Moulding Orthopedic Surgery. By Arthur Steindler, M. D., Professor of Orthopedic Surgery, State University of Iowa Medical School, Iowa City, Iowa. Cloth. Price, $4.50. Pp. 253, with 23 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., Oxford, England; The Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1949.

This book is attractively published. The quality of the paper and the type face make for easy reading. Following a short preface by the author are brief biographic sketches of Thomas, Jones and Ridlon. The main text is mostly excerpts from the writings of Hugh Owen Thomas, apparently selected to support the author's own theories on rest as a therapeutic agent. A supplement by Steindler of eighteen pages on Ridlon and his share in molding orthopedic surgery comprises the last chapter. This presents a clear picture of Ridlon's position in American orthopedic surgery. The book concludes with an annotated bibliography composed mainly of references to the writings of Thomas, Jones, Ridlon and the author.

Studies of Chronic Pyelonephritis with Special Reference to the Kidney Function. By Flemming Raaschou. Translated from the Danish by W. E. Calvert. Paper. Price, 20 Danish crowns. Pp. 260, with 61 illustrations. Ejnar Munksgaards Forlag, Nørregade 6, Copenhagen, 1948.

In the past fifteen years, as a result of the studies of Longcope and of Weiss and Parker, there has been wider recognition of the considerable frequency and great clinical importance of chronic pyelonephritis—a condition previously rarely diagnosed during life and often even misinterpreted at necropsy. This first presentation of detailed studies of renal function in chronic pyelonephritis by modern methods is a welcome addition to the literature on the disease, hitherto largely etiologic, anatomic and clinical. Included are systematic measurements of renal blood flow, glomerular filtration, iodopyracet tubular maximum (Tm), self depression and saturation limits for iodopyracet, urea clearance, urinary concentration and plasma protein fractions.

The monograph opens with a description of the results in 202 autopsies in which chronic pyelonephritis was present. Indicative of the frequency of chronic pyelonephritis is the fact that these constituted 5.6 per cent of all autopsies. Uremia was the cause of death in a third of the cases and hypertension in a sixth. Of special interest, the correct diagnosis was established during life in only 11 of 66 cases of chronic pyelonephritis sui generis; renal disease of any sort was diagnosed in only 21 of the 66 patients. The reviewer believes that the author's statement that clinicians do not have the disease sufficiently in mind also applies in this country.

The remainder of the book is devoted to a detailed study of renal function in chronic pyelonephritis. Renal blood flow, filtration and iodopyracet Tm are all diminished; the fall in iodopyracet is relatively greater than that in filtration. The numerous observations on glomerular and tubular functions do not yet appear to be of substantial value in the differential diagnosis of pyelonephritis or as a guide to treatment. However, they are of much interest to the student of the pathologic physiology of the kidney; as far as the reviewer is aware, similar data on renal function in pyelonephritis are not elsewhere available.

Kayne, Pagel and O'Shaughnessy's Pulmonary Tuberculosis: Pathology, Diagnosis, Management and Prevention. Revised and Partly Rewritten by Walter Pagel, M.D., Pathologist, Central Middlesex County Hospital, London; F. A. H. Simmonds, M.A., M.D., D.P.H., Medical Director, Clare Hall County Hospital, Middlesex, N. Macdonald, M.B., M.R.C.P., Physician to the Chest Clinic, Redhill County Hospital, Middlesex, and L. Fatti, F.R.C.S., Thoracic Surgeon, Hillingdon County Hospital and Harefield County Hospital, Middlesex. Second edition. Cloth. Price, $18.50. Pp. 720, with 268 illustrations. Oxford University Press, 114 Fifth Ave., New York 11, 1949; Amen House, Warwick Sq., London E.C. 4, 1948.

The second edition of this text book on tuberculosis is particularly welcome, for it has been considered a standard reference for information in the many fields concerned in tuberculosis. Since the printing of the first edition, in 1939, two of the original three authors, Kayne and O'Shaughnessy, have died. As the new authors point out, nine years is an unusually long interval in a period so fruitful in the development of knowledge of tuberculosis and so critical in the problems raised by tuberculosis in a world much of which has been devastated by war and famine. Originally the work was intended to combine in one volume a presentation of the pathologic, clinical and surgical aspects of pulmonary tuberculosis based largely on the individual conceptions of the authors, with the addition of essential references to general literature on the subject. This plan has been preserved in the second edition, which has been prepared by a group of authors who have worked closely with each other and with the remaining author from the original group. Thus, fortunately, the book does not represent a mere compilation of the literature, but rather the critical insight of a group of specialists on the many interrelated problems of the disease. In bringing it up-to-date they have in large measure rewritten the book and made it useful not only to specialists in the different fields of tuberculosis but to all who wish to inform themselves on developments in the understanding of pathogenesis and therapy. The principal development in studies on the pathogenesis of tuberculosis in recent years has been with respect to the origin and development of primary tuberculosis in adolescents and adults. There may be a difference of opinion with some of the conclusions, such as the statement that primary infection in adults is basically identical with that in childhood,

and some objection to the criteria for the diagnosis of primary tuberculosis in adults. So, too, in the opinion of many American pathologists and epidemiologists, the stress on the endogenous origin of tuberculosis in the adult may seem disproportionate. Dr. Pagel has studied a vast amount of material with great care, and his conclusions are correspondingly valuable. In the section on diagnosis, attention is called to the growing responsibility of private physicians in determining the activity of the many lesions of questionable significance detected in the course of mass roentgen surveys. It is unfortunate, but perhaps inevitable, that the section on chemotherapy of tuberculosis is far from up-to-date. Only five years have elapsed since streptomycin was first introduced in the therapy of tuberculosis, and no textbook requiring meticulous preparation over a period of years could possibly keep up with developments in this field. In this book the streptomycin treatment of tuberculosis is covered in an appendix, which gives an excellent review of advances in this field up to 1947. Another appendix serves a useful purpose in summarizing the classifications of tuberculosis used in Great Britain and the United States. The book is highly recommended to all students of tuberculosis both as a thoughtful and interesting compilation of established knowledge on the subject and as a stimulus to further work in less developed fields.

Introductory Foods. By Osee Hughes. Second edition. Cloth. Price, $4.25. Pp. 575, with 132 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1949.

Much sound, helpful general information on basic chemistry of foods is presented in this revision of a 1940 edition. Among specific chapters that have been expanded are those on food preservation and meal planning. Also, the number of illustrations has been increased, as well as the lists of recipes and methods of using them. Perhaps greatest appeal of the book so far as the physician is concerned is the calm, practical manner in which the author "debunks" the many popular superstitions regarding eating practices, such as the fear of eating foods that have been left standing in cans, the belief that white eggs are superior to brown eggs and the apparently widespread fear that aluminum cooking utensils are dangerous to health. Especially noteworthy is the discussion of coffee in a chapter on beverages. The subject of meats and meat cookery is handled in an outstanding manner in a special chapter.

Every conceivable aspect of food is included, with special chapters on frosted foods, salads and salad dressings, batters and doughs, food preservation, meal planning and meal service. In the last two, practical outlines are provided, with suggested meal patterns and special problems on marketing, utensils and work plans. At the close of each chapter are lists of suggested references for those interested in extended study. Compact data on weights and measures, temperature control in food preparation, definitions and descriptions of terms commonly used in food preparation, and general procedures are provided in four appendixes.

This volume can be recommended without reservation by physicians to patients interested in learning facts about food and its proper preparation. The book also provides a helpful brush-up for off the cuff answers to food questions, silly or otherwise, from patients.

The Hormones: Physiology, Chemistry and Applications. Volume I. Edited by Gregory Pincus and Kenneth V. Thimann. Cloth. Price, $13.50. Pp. 886, with illustrations. Academic Press, Inc., 125 E. 23rd St., New York 10, 1948.

The first volume of this two volume book is devoted to the information on hormones acquired relatively recently. It consists of chapters on hormones in plants, insects, crustaceans and mammals. The chapters are devoted to data on the chemistry and physiology of the endocrine secretions in plants and lower animals, the chemistry and physiology of the internal secretions of the parathyroid and pancreas, the physiology of lactation and mammary growth, the chemistry and assay of estrogens and the chemistry of androgens, progesterone and anterior pituitary hormones.

Volume II is concerned more with the physiology of the various mammalian hormones. Volume I contains a tremendous mass of data, much of which has been accumulated in the past ten years. The advances in the chemistry and physiology of the endocrines can not escape being most impressive when one compares the strides made during this period over the preceding ten years at the beginning of which endocrinology was in its infancy. The authors of the various chapters are recognized authorities on their respective subjects and are all major contributors to the experimental work in these fields. The volume is of classic academic proportions and should serve most valuably the research worker in endocrinology and the specialist in clinical endocrinology who is interested in maintaining an understanding of the basic developments in the field of hormones. Such readers would do well to peruse the chapters on the hormones of the lower animals and plants, which are both fascinating and instructive and may create additional stimulus to the scientific investigations in higher animals.

Les cahiers d'hématologie. Premier cahier: Le sang et les organes hématopoïétiques normaux. I: Cytologie descriptive; II: Techniques d'examen. Par Jacques Mallarmé et Jacques Messerschmitt. Paper. Pp. 158, with illustrations. Société d'Edition d'Enseignement Supérieur, 99 Boulevard Saint-Michel, Paris 5e, 1948.

This is the first of a series of publications on the study of normal and pathologic conditions of blood, under the editorship of Jacques Mallarmé and Jacques Messerschmitt; the plans may be somewhat pretentious. The pages are large (8½ by 11 inches); the typography is good, and the illustrations are interesting. There are five plates, two in black and white, and three in color. The color work is poor by our present day standards, but the plates amply illustrate the points of the text, and have probably been printed much more reasonably than would have been possible in this country. The text, evidently prepared for students and general practitioners, is elementary. This first number deals merely with descriptive cytology and technics. There is much lacking, and some of the researches of the past twenty years in this country are not mentioned. This is especially noticeable in the description of technics for the determination of hemoglobin. Mention is not made of the use of photoelectric colorimeters. A few technics developed in Europe recently and not familiar to us in this country, are described. For example, a diffractometric method of directly measuring the diameter of erythrocytes, which was devised by Tzanck and Bessis, is illustrated and briefly described.

For the American reader the chief interest of this series of publications will be as a work of reference to articles in the French literature on hematology.

Introduction to the Szondi Test: Theory and Practice. By Susan Deri. With a foreword by Dr. Lipot Szondi. Cloth. Price, $5. Pp. 354, with 19 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1949.

Psychiatrists and psychologists who are on the *qui vive* for the latest in psychometric technic have undoubtedly become acquainted with the Szondi Test which consists of 48 photographs of persons with a variety of mental diseases. Until Deri's book was published the only guide to the administration and interpretation of this test was Szondi's *Experimentelle Triebdiagnostik* which even in the hands of the skilled translator was found difficult to interpret.

Mme. Deri's contribution should not be considered a translation of Szondi's books. Comparatively little attempt has been made to present Szondi's theory of "the psychologic function of the latent recessive genes," which forms the basis for his test. For these, one must go to Szondi's "Schicksalanalyse." Instead, the present volume represents the author's attempt to interpret each of the basic test factors underlying this test. In addition, the psychologic assumptions contributing to this interpretation are indicated.

Whether or not one can go along with Szondi's hypothesis of the latent genetic factors which influence our spontaneous selection of photographs, Deri's presentation does evidence a good deal of plausibility, and in general her insistence on the interpretation of the selective reactions of subjects in terms of a constellation of related personality vectors appears to be sound.

The test itself is administered by supplying the subject with independent presentations of six sets of eight photographs. Each set contains a picture of a homosexual, a sadist, an

epileptic, a hysteric, a catatonic schizophrenic and a manic-depressive manic subject. As the subject is presented each set of eight pictures, he is instructed to select the two he "likes the most" and the two he "dislikes the most." Having gone through this process for each of the six series of photographs, the results are graphically recorded. The test is repeated at twenty-four hour intervals for six days or more. Time limits between tests are not absolute but should be within a day whenever possible.

The principles of interpretation stressed by Deri are briefly, these: (1) The eight diagnostic factors or categories in the test correspond to eight different "need-systems" in the subject. (2) The subject selects the photographs on the basis of the relationships between the factor represented in the photograph and his own need as reflected in psychodynamic tensions. (3) A high frequency of choices from one category represents a corresponding need in strong tension. (4) Low frequency or absence of selection of a category indicates freedom from a state of tension in that facet of personality.

Using these premises, Deri explains and interprets the various possible weighting of categoric choices. The interrelationships of the categories selected with each other are stressed, and the clinical use of the test is emphasized by the analysis of numerous profiles attained by subjects on this test.

This manual will prove useful to the serious worker with projective technics and is a great aid in overcoming the difficulties that some may have had with Szondi's own writings.

Atlas der Augenkrankheiten: Sammlung typischer Krankheitsbilder mit kurzen diagnostischen und therapeutischen Hinweisen. Von Dr. Rudolf Thiel, ord. Professor an der Universität Frankfurt a. M. Fifth edition. Boards. Pp. 225, with 634 illustrations. Georg Thieme, Diemershaldenstrasse 47, Stuttgart O, 1948.

This atlas, which first appeared in 1936, continues to be one of the best collections of colored illustrations of diseases of the eye. The reproductions are not as good, however, as in the first edition. One of the best features is a brief summary in each subject, which includes the anatomy, pathology and, in many cases, diagrams of operative procedures. This edition has a wealth of new material which will make it well worth while purchasing even for those who already have the first edition. It seems a shame that we cannot produce books of this sort in America without prohibitive cost.

The Basis of Chemotherapy. By Thomas S. Work, B.Sc., Ph.D., and Elizabeth Work, B.A., Ph.D. Cloth. Price, $6.50. Pp. 435, with 42 illustrations. Interscience Publishers, Inc., 215 Fourth Avenue, New York 3, N. Y.; Oliver & Boyd, Ltd., Tweeddale Court, 14 High St., Edinburgh 1, 1948.

The primary objective of the authors is "to focus attention upon the modes of action of drugs rather than upon the synthesis of ever more variants on their chemical structure." In this they have succeeded. They restrict the term chemotherapy to the chemical treatment of diseases of microbial origin. The authors have provided excellent background material which can serve as a basis for determining the rationale of chemotherapy. Stress is placed on the role of enzymes, which is consistent with current knowledge of drug action. Included are chapters on cell metabolism, essential metabolites, enzyme inhibition, drug antagonism, drug resistance and the relation of structure and activity of drugs. While much of the information may be too technical, the book nevertheless serves as a source of information for those who desire a better understanding of the role of chemotherapy in the control of disease.

An Elementary Atlas of Cardiography: An Introduction to Electrocardiography and X-Ray Examination of the Heart. By H. Wallace-Jones, M.D., M.Sc., F.R.C.P., E. Noble Chamberlain, M.D., M.Sc., F.R.C.P., and E. L. Rubin, M.D., F.F.R., D.M.R.E., Liverpool, England. Incorporating the third edition of "Electrocardiograms." Cloth. Pp. 108, with 100 illustrations. John Wright & Sons, Ltd., 42-44, Triangle West, Bristol 8, 1948.

This small volume is essentially all that is claimed for it. It is an attempt to minimize the detail the student should learn in this special subject. The description of electrocardiography and the illustrative electrocardiograms are sufficient to explain the basic principles. It probably is too elementary to appeal to the American medical student. The section on radiography of the heart and great vessels is well worth the student's time.

The 1948 Year Book of General Therapeutics. Edited by Oscar W. Bethea, Ph.M., M.D., F.A.C.P., Senior in Medicine, Southern Baptist Hospital, New Orleans. Cloth. Price, $4.25. Pp. 480, with 60 illustrations. The Year Book Publishers, Inc., 304 S. Dearborn St., Chicago 4, 1949.

Included in this volume are discussions of tests, new devices and technics, sulfonamide drugs, penicillin, streptomycin and other antibiotics, bacteriostatic agents, amebicides, antimalarials, antirheumatic drugs, antibodies and antigens, blood restoratives, vitamins, protein and amino acid therapy, hormones, anesthetics, sedatives, hypnotics and antispasmodics, antithyroid drugs, histamine and antihistaminic agents, drug treatment of headache, drugs acting on the heart and blood vessels and treatment of malignant conditions. Those who do not need an introduction to this book will find the current volume as useful as the preceding editions. Others who for the first time become familiar with this collection of abstracts or condensations of published articles and the accompanying editorial notes will find much useful information on current therapeutic procedures.

Die Permeabilitätspathologie als die Lehre vom Krankheitsbeginn. Von Prof. Dr. Hans Eppinger. Cloth. Price, 29.40 schillings. Pp. 755, with 145 illustrations. Springer-Verlag OHG, Möikerbastei 5, Wien 1, 1949.

This book represents a much enlarged edition of the previously published monograph of this author on serous inflammation. Additional observations include studies with fluorescent microscopy, investigations on hepatic diseases derived from experiences during the war and studies on renal diseases. In the original publication, considerable emphasis was placed on the escape of plasma proteins into the tissue spaces and on the sequelae supposedly resulting from this escape. Much importance was attached to this serous inflammation (a name derived from Roessle) in various parenchymal organs. In the present enlarged treatise, in addition, the invasion of the parenchymal cells themselves by plasma proteins is stressed. These shifts in plasma proteins caused by altered permeability of the cellular membranes and capillaries are considered important in the pathogenesis of many diseases. Disturbances of the permeability of cellular and capillary membranes are considered the initial processes of many pathologic conditions. Morphologic and functional alterations in renal, hepatic, cardiac, gastrointestinal and rheumatic diseases are cited as examples. The study contains much useful information derived from various clinical, histologic and experimental observations. Many of the conclusions are a tribute to the originality of the author. Others, however, are based on assumptions and speculations rather than on correct interpretation of experimental and clinical observations. This final work of Eppinger, which appeared after his death, may stimulate thinking and investigation in various fields, as did his previous publications.

Posttraumatic Epilepsy. By A. Earl Walker, M.D., Professor of Neurological Surgery, The Johns Hopkins University, Baltimore, Md. Publication Number 20, American Lecture Series. A Monograph in American Lectures in Surgery. Cloth. Price, $2.75. Pp. 86, with 20 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., Oxford, England; The Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1949.

This is an excellent short account of an approach to focal cerebral seizures resulting from trauma in adult life. Dr. Walker was charged with the surgical treatment of seizures among the war wounded of the United States Army, and this volume is largely a condensation of that experience. The scope of the book does not therefore completely fulfil its title, and some aspects of post-traumatic epilepsy (in particular those referring to injury at birth or in childhood) are omitted. This in no way detracts, however, from the way the author has treated the material.

After stating the problem and discussing factors of etiology and pathogenesis, the author gives an account of the electrographic manifestations of this disorder. He has perhaps approached these with more insight than he has the clinical aspects of the attacks. Chapters on medical and surgical management are well done, and the latter alone would justify the book.

The monograph will find wide appeal among both students and practitioners and among those more intensively occupied with the problems of focal epilepsy.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DISCOMFORT FOLLOWING BOWEL MOVEMENTS

To the Editor:—**A 30 year old white woman complains of nausea, abdominal discomfort and slight flatulence following bowel movements. Her bowel movements are fairly infrequent (i. e., every four or five days). The distress comes after variable periods of time following evacuation, or even just prior to the time, and lasts about twenty-four to forty-eight hours. Other symptoms are occasional sharp pain in the chest and bilateral headaches. The patient is thin and inclined to be nervous. She frequently becomes tearful for no apparent reason. There does not seem to be any current emotional disturbance or conflict. Results of physical examination are normal except for lateral displacement of the uterus, as indicated by the pointing of the cervix toward the patient's right and visceroptosis for which she wears a spinal appliance with no appreciable relief. The basal metabolic rate is — 30 per cent. The patient is getting thyroid. The blood cell count reveals slight anemia, and liver and iron are being given by mouth and injection.** M.D., Pennsylvania

ANSWER.—It seems clear that at least one problem is the patient's unstable emotional makeup. Whether this is the only problem remains to be established. Complete diagnostic studies should be performed, including roentgenograms of the chest, stomach and colon, examination of the stools for occult blood with the patient on a meat-free diet and a proctoscopic examination. If the history or neurologic observations suggest an organic explanation for the headaches, roentgenograms of the skull, visual field measurements and spinal fluid examination may be necessary. If there are no significant findings, symptomatic therapy should be administered. The spinal appliance may be discarded, for the visceroptosis is undoubtedly unimportant. Surgical measures to correct the displaced uterus are to be avoided. A bland, low residue diet should be given, along with a sedative and an antispasmodic, such as phenobarbital, 0.015 or 0.03 Gm., and extract of belladonna, 0.0075 Gm., three or four times daily. Reclining for half an hour or so with a heating pad applied to the abdomen after bowel movements may make the patient more comfortable. Although myxedema may not be present, it will probably do no harm to continue small doses of thyroid extract for the present.

The psychiatric aspects should be investigated further.

AURALGAN® IN CHILDREN

To the Editor:—**I am concerned over the widespread use of auralgan® (about 6.3 Gm. antipyrine and 1.7 Gm. ethyl aminobenzoate in 100 cc. dehydrated glycerol) for the elimination of ear ache in children. Is there a transformation of the normal tympanic sheen and if so how does this affect further examination of the drum? Can an ear drum rupture painlessly because of the use of auralgan® and would such morbidity be considered preventable? Does an ear drum which has ruptured spontaneously prove to be more susceptible to reinfection during future infections of the upper respiratory tract?** Vincent E. Romano, M.D., Bristol, Pa.

ANSWER.—Auralgan® will somewhat diminish the normal tympanic membrane sheen. This must be taken into consideration when evaluating the progress of an otitis media in which auralgan® has been used. The use of the preparation would not be likely to increase the probability of spontaneous rupture of the tympanic membrane. The fact that an ear drum ruptures spontaneously does not in itself increase the susceptibility of that ear to future reinfection. However, early spontaneous rupture might indicate high virulence of the infecting organism or poor ability of the patient to combat the infection. The likelihood of reinfection is increased by the presence of local predisposing factors such as obstructing lymphoid tissue at the tubal orifice, sinusitis or allergy.

SENSITIVITY TO COTTONSEED

To the Editor:—**Is a patient who shows a positive skin reaction to cottonseed likely to be sensitive to foods made from cottonseed oil?** M.D., Ohio

ANSWER.—The question of whether or not cottonseed oil will be tolerated by the cottonseed-sensitive patient (as based on the evidence of skin tests) is not yet a completely closed matter. The evidence indicates that cottonseed oil should be and presumably is free from cottonseed protein residue capable of inducing an allergic reaction in most, if not all, cottonseed-sensitive patients.

CANCER OF THE THYROID

To the Editor:—**Pleaes let me know the status of isotopes in the treatment of cancer of the thyroid? In a woman 26 years of age, I found a small adenoma with some invasion of the adenoma capsule. It was diagnosed as papillary adenocarcinoma grade I. I did a subtotal lobectomy, the adenoma being surrounded by thyroid tissue. Do you feel that there is any further treatment necessary in such a case?** R. E. Jernstrom, M.D., Rapid City, S. D.

ANSWER.—Iodine ^{131}, the eight day isotope of iodine, appears to be the treatment of choice for carcinoma of the thyroid gland, particularly if there are known metastases. Early workers were frequently disappointed with the action of this agent because of failure of the metastatic tissue to collect radioiodine in sufficient concentration. Continuing studies have shown that several measures may influence this condition favorably. The most promising results have been obtained with the use of the thyrotrophic hormone of the pituitary, preliminary ablation of the thyroid gland and repeated administration of large doses of radioiodine even when evidence of good concentration is lacking.

With respect to the case cited, there does not appear to be any indication for further therapy at present. In general, thyroid adenomas of the type described tend to be well circumscribed, largely benign lesions. The extensive resection with demonstrable normal tissue surrounding the tumor should be adequate therapy. Most workers with experience in the use of radioiodine would not advise it for such a patient. "Tumor doses" of radioiodine would necessarily produce complete myxedema. This result would be acceptable only when a highly malignant tumor was present; it would not be justifiable in the patient described.

RHINITIS FOLLOWING EXPOSURE TO NEWSPAPERS

To the Editor:—**A 43 year old patient has vasomotor rhinitis whenever he reads a newspaper. Magazines which have paper with a smooth finish do not cause any symptoms. Desensitization with house dust has given him some relief. Is there anything in the paper used in newspapers that is not present in that used in magazines which might cause allergic symptoms of this kind?** M.D., New York.

ANSWER.—The type of manifestation described is not uncommon on exposure to newspaper, although skin reaction to extracts made from the paper and to some of the inks used in printing may be negative. There are several possible explanations of this discrepancy: The proper raw materials may not be available for testing; manufacturers hesitate to discuss their processes and ingredients, and thus the testing materials available may be incomplete; the substance to which the patient is allergic may not produce a skin reaction, which is particularly likely if the allergenic substance is a simple chemical rather than a protein, and the substance producing the symptoms may be a chemical irritant rather than an allergen. In other words, the patient may be showing an allergic response to another substance, from which he normally has little, if any, trouble. In this instance, the exciting factor disturbs the tissues, thus acting as a nonspecific cause in precipitating signs of allergy.

The second possibility offers the most likely explanation. Occasionally the vegetable gum used in the spray for drying the ink may be responsible for allergic symptoms. This explanation, however, does not apply in the majority of cases. Information on the differences between ingredients of newspapers and magazines are not available. However, it is doubtful that there is a distinct difference in patients' reactions because of such differences. It is more likely that the freshness of the one as compared with the age of the other is the relevant difference, since it is a common experience that patients complain of symptoms from fresh newspapers and frequently say that they can read old ones without ill effect.

POSSIBLE MENTAL RETARDATION

To the Editor:—**A 3½ year old boy does not speak but appears intelligent. He makes noises to direct attention, cries loudly when hurt and has a vicious habit of biting his playmates. He has a history of epileptiform seizures, during which he froths at mouth, has convulsive movements of his limbs and becomes unconscious. His attacks are preceded by screaming.** M.D., New York.

ANSWER.—The repeated convulsions require the diagnosis of epilepsy, and the failure to speak without deafness suggests mental retardation. Both might be the results of congenital brain defect or of some acquired condition, such as birth injury or encephalitis. Additional items of evidence needed for establishing a cause are: family history of epilepsy or of mental defect, personal history of brain damage, electroencephalogram and examination by a child psychologist.

TRICHLOROETHYLENE POISONING

To the Editor:—A 28 year old industrial worker complains of anorexia, weight loss and burning of the hands and feet. Results of physical examination, blood cell count and urinalysis are within normal limits. He has been working on a "degreasing" operation, using a degreasing solvent which apparently has trichloroethylene as its base. The burning of his hands increases when he gets close to the vapor (he does not wear gloves). The present symptoms are of three weeks' duration, although he has worked with the solvent on and off for the past year. What are the symptoms of industrial trichloroethylene poisoning, and are this man's symptoms compatible? M. D., Ohio.

ANSWER.—Trichloroethylene ($CHCl:CCl_2$) is a chlorinated hydrocarbon of known toxic properties; it is about one half as toxic as carbon tetrachloride or chloroform. After exposure to vapors at concentrations above (about) 100 parts per million, there may promptly arise dizziness, nausea, vomiting, headache, impaired coordination and a general state similar to alcoholic intoxication. Loss of weight due to anorexia may appear in time. Usually, manifestations are acute and fleeting, but on rarer occasion damage may be wrought on the liver, kidneys and heart. The chief point of attack is the central nervous system, and unconsciousness may promptly arise from gross exposure. The temporary action of this substance is indicated by the fairly widespread practice of using trichloroethylene as a general anesthetic, such as in obstetric delivery. In high concentrations this chemical will degrease or defat the skin, paving the way for dermatitis. There is some reason to believe that passage through the intact skin may take place, so that protection of inhalation may not fully insure its not entering the body. The mentioned manifestations may represent a mild degree of damage from the substance under discussion. The fact that symptoms appeared only three weeks before the date of inquiry (June) is in keeping with the observation that vaporization is facilitated in hot weather. The standard equipment of the company is of high order, but however well operated and maintained the equipment, some escape of vapors may arise. The Ohio State Department of Health is qualified and equipped to make suitable tests for determining the exposure level to trichloroethylene in varying work circumstances.

VITILIGO

To the Editor:—Is there any way to prevent a small depigmented area of skin from spreading to a large area. In this particular case, there are large areas on the trunk and a small area is starting on the face.

Karlton H. Kemp, M.D., Texarkana, Ark.

ANSWER.—This is undoubtedly a case of vitiligo. The disease tends to progress to a certain point and then remain more or less stationary. It is impossible to predict the final extent of the depigmentation in any patient. Treatment has been unsatisfactory. Use of ultraviolet rays, especially with the water-cooled lamp, has been reported successful in some cases. Use of ultraviolet rays together with gold salt solutions intravenously have helped others. Still other methods which have caused improvement at times are freezing with solid carbon dioxide and the application of 10 per cent alcoholic solution of bergamot oil together with exposure to ultraviolet rays. The lesions may be made less noticeable by bleaching the hyperpigmented borders. The depigmentation may be masked by applications of dilute solutions of walnut juice or similar preparations. It may be best to treat the patient by convincing him that the disorder is neither harmful nor objectionable.

CUNNILINGUS

To the Editor:—A married female patient is concerned about the morality of cunnilingus. This act is performed on the patient by her husband at his wish at infrequent intervals as part of preliminary "love play" and is followed by normal intercourse. She admits that the practice is pleasurable, but she feels considerable guilt that it is one of perversion and has asked my opinion. This matter is not discussed at any length in any of the books at my disposal. What is the concensus in this matter? M.D., Colorado.

ANSWER.—Considered from the point of view of psychopathology cunnilingus should not be regarded as a perversion or abnormal if it is a part of the forepleasure or preparation for normal intercourse and not a substitutive act. From the moral standpoint the sense of guilt in connection with it arises from the common feeling that the sexual parts, no matter how completely cleansed, are still unclean rather than from any essential immorality of this practice when it is only a part of the love-making of a married couple preparatory to normal intercourse.

TASTE ABERRATION AND SORE TONGUE

To the Editor:—I have a patient 60 years old who complains of a salty, bitter taste in her mouth and a sore tongue of two years' duration. I am unable to see anything on her tongue. I have given her phenobarbital, triple bromides and vitamin B complex. Please let me know what to do.

J. O. Helm, M.D., New Florence, Mo.

ANSWER.—The points which should allow a diagnosis to be made are a sore tongue and a taste aberration of two years' duration in an apparently healthy woman aged 60 years, with no visible signs of pathologic changes of the tongue. If the tongue is actually sore and tender, glossitis is indicated; if the word "sore" means soreness or burning, there need not be a local cause for the symptoms. The salty, bitter taste could be due to glossitis, with its local effect on the taste buds. It may occur with little or no inflammation. The most probable local causes of such glossitis are a vitamin deficiency, a dental change and/or a low grade infection.

The vitamin deficiency is almost invariably of the B complex; it may be multiple, with a lack of thiamin, riboflavin, nicotinic acid or B_{12} factors. One should first test for pernicious anemia by a blood cell count and an analysis of the gastric acidity (including the use of histamine); suitable treatment, with a liver extract or the newer vitamin B_{12}, can then be used if indicated. If a secondary microcytic anemia and achlorhydria are present, the condition could be achlorhydric anemia. It is also possible to have anemia and glossitis, due to iron deficiency, which responds to administration of iron. The diagnosis of deficiency of other factors of vitamin B complex can be made on the basis of a diet history or a therapeutic test; full doses of a vitamin B complex concentrate can be given orally or parenterally for at least three weeks to determine the effect. Sevringhaus obtained fine results by giving nicotinic acid for three weeks, 50 mg. or more per day orally.

A burning sensation and eventual glossitis may follow the introduction of a new denture or denture cleanser or may be caused by the presence of a new filling with a different amalgam (and a resultant irritating electric current in the mouth). These points can be determined by a more extensive history and corrected by removal of the fault. An infectional cause can also best be excluded or identified by a dentist. Other local causes of a burning type of soreness are excessive smoking or a functional decrease in the amount of saliva.

If the symptoms are present without any of the aforementioned causes and if a trial of therapy fails, or if the "soreness" is purely a sensation, there may be a psychoneurotic cause. The patient's emotional status or history (not mentioned) may suggest this from the start. The type of disorder might be menopausal, situational or hysterical and could be best determined and treated by a neuropsychiatrist.

PREVENTION AND TREATMENT OF ERYTHROBLASTOSIS

To the Editor:—Can erythroblastosis fetalis be prevented? What is the best treatment of this condition? M.D., Pennsylvania.

ANSWER.—Transfusion of Rh-positive blood to an Rh-negative woman may sensitize her. If she then becomes pregnant with an Rh-positive fetus the sensitization may become reinforced and the infant may have fetal erythroblastosis. Intramuscular injections of Rh-positive blood may have an effect similar to that from a transfusion especially if repeated injections are given. Sensitization by transfusion or injections may persist for many years. Therefore, girls or women must be tested for their Rh factor before transfusions or injections of blood and if found Rh-negative should receive Rh-negative blood. At the present time this is the only means of prevention of erythroblastosis. Carter (Rh Hapten: Its Preparation, Assay and Nature, *J. Immunol.* **61**:79-88 [Jan.] 1949) reported recently that injection of Rh hapten during pregnancy may prevent erythroblastosis. However, this claim must await corroboration.

Transfusion of Rh-negative blood has been found effective in the treatment of the erythroblastotic infant. Ten cubic centimeters of blood per pound of body weight is recommended. The transfusion has to be repeated one or more times, depending on the condition of the infant. Good results have been observed following transfusion of washed Rh-negative red cells suspended in 5 per cent dextrose solution. In some instances so-called exchange or replacement transfusion has been found useful. Small amounts of blood (from 20 to 30 cc.) are withdrawn from the infant and somewhat larger amounts of Rh-negative blood (of the same group as the infant's or of group O) are injected until about 420 cc. has been removed and 500 cc. injected. The umbilical vein is used most frequently. This route can be used for only about 10 hours after birth, as the vein closes soon after birth. The femoral vein also can be used and is not subject to time limitation. The longitudinal sinus and

the radial artery have been recommended for removal of blood and any of the commonly used veins (temporal or cubital) for the injection. When one of these two routes is used, one does not have to alternate the withdrawal and injection of blood and both may proceed simultaneously. (Diamond, L. K.: Replacement Transfusion as a Treatment for Erythroblastosis Fetalis, *Pediatrics* **2**:520-524 [Nov.] 1948. Wallerstein, H.: Substitution Transfusion: A New Treatment for Severe Erythroblastosis Fetalis, *Am. J. Dis. Child.* **73**:19-33 [Jan.] 1947. Wiener, A. S., and Wexler, E. B.: Results of Therapy of Erythroblastosis with Exchange Transfusion, *Blood* **4**:1-35 [Jan.] 1949.)

Oxygen therapy is especially useful until the anemia has been corrected.

It has been claimed that erythroblastotic infants should not be nursed by their mothers. According to recent studies this restriction is not warranted, because there is no evidence that Rh antibodies can pass through the gastrointestinal mucosa of infants.

Transfusion therapy applies also to erythroblastosis due to A or B blood group incompatibility. Blood of group O should be used, and the Rh factor of the transfused blood should be the same as the infant's.

HABITUAL ABORTION

To the Editor:—A woman who wants a child has had three miscarriages in five years, each miscarriage occurring at two months. Her menses were always so painful that she had to go to bed for one day, but they were of normal length and quantity and free from clots. She is 5 feet 4 inches (163 cm.) tall and used to weigh 150 pounds (68 Kg.). The last five months she had taken ½ grain (33 mg.) thyroid daily and her weight has been reduced to 140 pounds (64 Kg.). She just had her third pregnancy and had received progesterone during what would have been her menstrual week. Her brother and one sister both have healthy children, and her family seems healthy and prolific. Her husband is a clerical worker, weighs about 200 pounds (91 Kg.) and seems healthy. Do you have any suggestions? Results of Kahn tests are negative for both husband and wife.

John A. Kittelson, M.D., Sioux Falls, S. D.

Answer.—This woman belongs in the class of women who abort habitually, and her trouble is not easy to correct. A thorough examination should be made of both husband and wife. Both patients should have one or more basal metabolism studies, and if the basal metabolic rates are low, thyroid extract should be prescribed. Both husband and wife appear to be overweight. Nothing is said about whether a curettement was performed after the abortions, but presumably it was not performed. Sometimes dilatation of the cervix and curettement is helpful.

Apparently this patient has no difficulty in conceiving. As soon as she misses a menstrual period, she should be advised to take 10 mg. of diethylstilbestrol every night. She should also be advised to stop all sexual intercourse, all travel in buses, autos or streetcars and to leave the house only when necessary. For the week during which the menses would have occurred were the patient not pregnant, she must remain off her feet except to go to the toilet. About two weeks after the missed menses a pregnandiol test should be made to determine whether there is a deficiency of progesterone. If there is a pregnandiol deficiency, 75 to 100 mg. of progesterone should be given hypodermically every day. This, however, is expensive. The diethylstilbestrol should be continued, but each week after the first four weeks the dose should be increased 5 mg. daily until 35 mg. a day is taken. This dose should be maintained until the end of the seventh month. The progesterone should be continued only as long as repeated frequent pregnandiol tests reveal the need for this therapy. At least 1 to 2 grains (65 to 130 mg.) thyroid extract daily should be given if the basal metabolic rate is low.

WATER SOFTENERS AND PRURITUS

To the Editor:—Information regarding water-softening processes as a cause of pruritus would be appreciated. If this is a recognized cause, is it an allergic manifestation?

M.D., Fla.

Answer.—The chemicals employed in water softening foremostly are determined by the volume of water to be softened. At the municipal level such substances as sodium carbonate and calcium oxide may be found. At the village level the zeolite processes may be utilized, the chief chemical being hydrated sodium aluminum silicate. At a slightly lower level, water softening may be brought about through the action of various phosphates—among others the sodium pyrophosphate. At the laboratory level exchange resins may be utilized to produce water of almost distillation purity. In any situation, pruritus is most likely to arise when the active agent is an alkali. The alkali acting on the skin tends to destroy the normal acid mantle. "Winter itch," a highly common skin disturbance, arises from a similar cause. Harsh soaps yielding considerable alkali on hydrolysis deprive the skin of its normal acid state. It is more common during winter months, since during that period the outpouring of perspiration acid is at a low level. Usually the pruritus that may arise from alkali water softeners is not associated with allergy but, instead, represents an early stage of dermatitis. In fact, frank dermatitis from contact with water-softening agents may arise.

TETANUS IMMUNITY

To the Editor:—In reference to the query on "Tetanus Immunity" in The Journal (page 758, June 25, 1949), the following comments appear to be urgently indicated. Tetanus, as it occurs in human beings, is not an immunizing disease. The evidence for this statement is immunologic and clinical. With respect to the former, titration of specimens of blood obtained from patients at variable intervals after the injection of graded quantities of tetanus antitoxin reveals a gradual, but ultimately complete, disappearance of specific antibodies from the circulation. This situation prevails in both normal persons and persons who have experienced clinical tetanus. Other conditions being equal, the rate of elimination is governed by the amount introduced (Madsen, T.: The Decrease of Antibodies in the Organism Indicated by a Formula, in Festskrift ved indvielsen af Statens Serum Institute, Copenhagen, O. C. Olsen & Co., 1902, no. 8). In general, the following rule is a reasonably accurate guide: 1,500 American units (an American unit is twice the International unit) confer titrable immunity for two to three weeks, 10,000 units for six to ten weeks and 100,000 units for eight to eleven weeks or sometimes longer (Cooke, J. V., and Jones, F. G.: Duration of Passive Tetanus Immunity and Its Effect on Active Immunization with Tetanus Toxoid, J. A. M. A. **121**:1201 [April 10] 1943). In respect to higher doses, such as the 500,000 units described in the query, the serial titers of a patient who received 1,254,000 International units (627,000 American units) over a period of eleven days (almost all by the intramuscular and subcutaneous routes) have been reported (Sohier, R., and Jude, A.: *Bull. et mém. Soc. méd. d. hop. de Paris* **54**: 80, 1938). The titers were as follows: 30 to 50 units per cubic centimeter on the sixth day after the termination of specific serotherapy, 3 to 30 units on the fifteenth to the thirty-ninth day and between 0.01 and 0.03 unit on the eighty-sixth to the one hundred and sixth day. The clinical information consists of authenticated reports of multiple attacks of tetanus in the same person (Behring, E.: *Schmidt's Jahrb.* **340**:1, 1915. Sick, cited by Brandt, H.: *Zentralbl. f. inn. Med.*, **36**:565, 1915). During the later attacks there has been no consistent tendency toward modification of the disease, and a fatal outcome may occur (Westwater, A. M.: *Brit. M. J.* **1**:395, 1917). Single or multiple attacks of tetanus supply neither basic nor humoral immunity. Consequently, patients who have survived one or more attacks of the disease require the same artificial antigenic stimulus (tetanus toxoid) as do those who have not had tetanus. The superiority of the artificial over the natural antigenic stimulus is purely a matter of dosage. In the natural disease, one minimal lethal dose (M. L. D.) is fatal. When tetanus toxin is converted into toxoid, multiples of a lethal dose may be injected without causing clinical tetanus.

Tetanus toxoid must be injected at an appropriate interval after antitetanic serum. The duration of titrable immunity after variable amounts of tetanus antitoxin has already been described. In this respect, it is pertinent that the disappearance of the inhibiting effect of passively received antitoxin (antitetanic serum) is more important in the early development of active immunity than the time at which the injection of tetanus toxoid is started (Cooke and Jones, see previous reference). Consequently, the time of administration of tetanus toxoid (preferably three injections of refined alum-precipitated toxoid at intervals of two to four weeks) is to be governed in terms of the amount of antitoxin originally injected. Obviously, this applies also to the follow-up active immunization of a patient who has received a prophylactic dose of tetanus antitoxin following an injury considered likely to lead to the appearance of the disease. In this respect, it is pertinent that the general trend is in the direction of employment of prophylactic doses of 5,000 to 10,000 American units instead of 1,500 units. Moreover, it may be restated that the first dose of tetanus toxoid should be administered about six weeks after 10,000 American units of tetanus antitoxin.

Concerning the large dose of antitoxin described by the writer of the query, it is significant that doubt prevails concerning the therapeutic value of antitetanic serum. In fact, the administration of antitetanic serum to a patient acutely ill with tetanus is fraught with danger. During the period of accelerated or delayed serum sickness, reactivation of convulsions may occasion sudden death. Moreover, statistical evidence of a convincing nature is lacking to validate the routine employment of tetanus antitoxin as a therapeutic agent. The use of antitetanic serum continues to be of cardinal importance for the prophylaxis of tetanus. When used, adequate amounts (5,000 to 10,000 units or more on certain occasions) are mandatory. Moreover, follow-up active immunization with tetanus toxoid is obligatory, in order to spare the patient the possible dangers of acute, subacute (accelerated) or delayed serum sickness. It is to be emphasized that criticism of the therapeutic value of antitetanic serum in no way means that antitetanic serum should be ignored in the prophylaxis of this disease.

Critical evaluation of the various dosage schedules employed in the serotherapy of tetanus indicates that amounts of 40,000 to 60,000 units, administered as one dose (intramuscular or intravenous) are associated with mortality rates no higher than those following the employment of the larger quantities (Spaeth, R.: Serum Therapy of Tetanus, *Am. J. Dis. Child.* **61**:1146 [June] 1941).

Immunologic and clinical data are lacking to indicate that foreign protein reactions, related to the injection of tetanus toxoid (which contains no horse serum) into a patient previously inoculated with tetanus antitoxin, do or should occur. Acceptance of such a point of view would invalidate the basic concept of the specificity of allergic phenomena.

Ralph Spaeth, M.D., Chicago.